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WORK OF THE ANAESTHESIOLOGY CENTRE IN COPENHAGEN

In most countries, anaesthesiology first began to emerge as a separate discipline about twenty years ago, and there was soon a serious shortage of personnel trained in the new specialty. In 1950, the Danish Government and the University of Copenhagen requested the assistance of WHO in establishing an international training centre in Denmark. This assistance was provided in the form of instructors and fellowships for trainees from other countries, but gradually the Danish Government has taken over more and more of the responsibility for the course, and it is expected that within a few years it will become an entirely national project. In spite of a number of shortcomings which experience has revealed, the courses have served a valuable purpose, and 179 anaesthetists from 29 different countries have been trained in seven years. In the article below, Dr E. Wainø Andersen, Chief Anaesthetist, Copenhagen County Hospital, describes some of the work—and some of the difficulties—of the centre.

It was in the years 1947-1949 that the new specialty of anaesthesiology began to gain official recognition in Denmark and the first full-time hospital posts for anaesthetists were created in the university towns of Copenhagen and Aarhus. In the USA, Canada and the United Kingdom, rapid advances were being made, particularly in the techniques of administering anaesthetics, but in Denmark, as in other European countries, large quantities of anaesthetics were still being given by untrained surgeons, theatre sisters, and nurse anaesthetists who were more or less self-trained. There was, in fact, an almost complete lack of trained anaesthetists in Denmark.

In this situation, Dr J. Frandsen, Director-General of the National Health Service of Denmark, decided to seek the assistance of WHO in setting up a centre to provide facilities for international training in anaesthesiology. Through Professor E. Husfeldt, surgical adviser to Dr Frandsen, the co-operation of the University of Copenhagen was also ensured, and the centre was established at Copenhagen on 1 May 1950. With the assistance of WHO it was possible to recruit instructors of the highest international standing—mainly from the United Kingdom and the USA—for the first year's course, and WHO also provided fellowships for non-Danish trainees, in addition to placing certain literature and equipment at the disposal of the centre.

Anaesthesiology as a public health concern

It has been said that the main concern of WHO is with problems of public health and preventive medicine, and that anaesthesiology does not properly belong in these categories. As Dr E. Kohn, Chief, Exchange of Scientific Information Section, WHO, has pointed out, however: " . . . if we bear in mind that properly conducted anaesthesia prevents many a complication in the operating room and in the post-operative period, then the preventive aspect is rather obvious. One may say that there are very few diseases, indeed, that have the incidence of surgical operations . . . and anaesthesiology thus becomes an effective means in the prevention of disease and death in situations that are often as inevitable as disease itself . . . "[1] On the other hand, improperly administered anaesthetics can

[1] Kohn, E. (1951) In: *Proceedings of the First Congress of the Scandinavian Society of Anaesthesiologists, 1950*, Copenhagen

cause death or disability. Beecher & Todd [2] have reviewed the position in the USA and conclude: "Anaesthesia might be likened to a disease which afflicts 8 000 000 persons in the United States each year. More than twice as many citizens out of the total population of the country die from anaesthesia as die from poliomyelitis. Deaths from anaesthesia are certainly a matter for 'public health' concern."

It should perhaps be pointed out here that the administration of anaesthetics during operations is only one of the functions of a modern anaesthetic service. During the tragic epidemic of poliomyelitis in Denmark in 1952, new methods of treatment were developed simply by transferring the operating room techniques of the anaesthetist to the medical wards. Following this experience, the advice of the anaesthetist has been sought in many different branches of medicine, and this has been largely instrumental in revising previous concepts regarding the treatment of tetanus, certain cardiac and pulmonary diseases, cerebrovascular accidents, paediatric diseases and various types of injury. Recently an entirely new approach has been made to the whole question of the transport and resuscitation of poisoned, asphyxiated and severely injured patients. In these ways, too, anaesthesiology is making its contribution to public health.

Functions of the Copenhagen training centre

It has never been the aim of the centre to offer a complete training in anaesthesiology. Post-graduate clinical training takes an absolute minimum of six years. In Denmark, for example, the requirements are: clinical practice for one year, medicine (pharmacology or physiology) for one year, surgery for one year, and clinical anaesthesia for three years. In other European countries, the curriculum is similar. The course at the Copenhagen centre lasts one year, and it is therefore legitimate to ask what purpose it serves. Is it intended to offer basic training for physicians having no previous knowledge of anaesthesiology, moderately advanced training for physicians already having some knowledge of the subject, or advanced training in the most recent concepts of anaesthesiology for specialists? Looking back, the most truthful reply seems to be that the centre has made some attempt to do all these things without doing any of them properly. The main reason for this lies in the heterogeneous nature of the "class" at any one of these courses. Not only are the trainees drawn from many different countries, but they also differ widely in their previous experience in anaesthesiology. Of those attending the seventh course, for example, two were expert anaesthetists, two had never given an anaesthetic before, and the rest had either trained themselves or received some kind of instruction.

By force of circumstances, therefore, the courses have had to be designed with as wide a scope as possible in order that all the participants might benefit from them. Those who have had no previous experience receive a basic training and are enabled to judge whether they wish to continue their specialization; if so, they may be given advice on how to plan their future training, possibly with financial and moral support from WHO. Trainees with previous knowledge of anaesthesiology have the opportunity of studying a number of different techniques, in addition to supplementing their theoretical knowledge, and they are able to profit from contact with some of the leading specialists in the field. Those who are already specialists are given a chance to delve more deeply into certain problems, and may be granted follow-up fellowships by WHO for specialized training in other countries.

Organization and programme

Considerable emphasis is placed on the desirability of presenting to the trainees a variety of schools of thought. This is achieved in two ways: by inviting foreign consultants to be responsible for part of the instruction, and by a system of rotation between hospitals for the practical training. Six Copenhagen hospitals are co-operating with the centre, and visiting trainees usually

[2] Beecher, H. K. & Todd, D. P. (1954) *Ann. Surg.*, **140**, 2

spend about two months in each. Danish trainees are attached to the same hospital for the whole year of the course, as they are able to visit the other hospitals during their normal specialist training. Whenever possible, the teaching programme is supplemented by instructive films, by special demonstrations in one of the hospitals, and by visits to laboratories, hospitals not participating in the course, and factories producing drugs, oxygen or anaesthetics. Once a year, the whole group of visiting trainees and Danish instructors pays a visit to a number of Danish provincial hospitals.

The practical teaching at the different hospitals is by no means uniform, of course. One hospital may be in favour of using cyclopropane in the majority of cases, another may recommend nitrous-oxide-oxygen-curare-ether sequences, while a third may place the main emphasis on local and regional anaesthesia. This has disadvantages for the beginner, but it enables the more advanced trainee to gain a first-hand knowledge of a variety of methods and form his own judgement as to their relative merits; it also underlines the fact that the same end may be achieved through different means, and that good results depend more on sound technique than on choice of method.

On the theoretical side, the course has so far offered about 120 lectures, covering all aspects of anaesthesiology, including related topics in the fields of surgery, internal medicine, neurology, radiology and serology. Short courses in physiology, pathology and pharmacology are also given, subject to the availability of lecturers. From the beginning of the eighth course, in February 1958, the theoretical instruction was intensified in order to bring the inexperienced trainee as quickly as possible to the stage where he can derive the maximum benefit from the course. Some of the hospitals offer additional theoretical and clinical training on a basic level to smaller groups.

Within the last seven years, 39 visiting consultants have been selected from among the best anaesthetists in England, the USA, and the Scandinavian countries. Practically every one of these consultants has had his own special sphere of interest and, although they may sometimes have held diametrically opposite views on certain points, this has again helped to give the trainees a broad outlook. Some of these consultants have held informal tuition sessions, which have been greatly appreciated.

The problem of language has not been, and probably cannot be, completely solved. Instruction is given in English, but it has proved almost impossible to find out in advance whether an applicant's knowledge of this language is adequate to enable him to follow the course. On the other hand, it has happened that a trainee whose knowledge of English at first appeared to be quite insufficient afterwards turned out to be an excellent anaesthetist with the sort of enthusiasm for the new specialty that made him a pioneer when he returned to his own country. Another language difficulty is that the majority of trainees, having no knowledge of Danish, are unable to communicate with the patients.

The results

During the period May 1950 to January 1958 the course has been attended by 179 trainees from 29 different countries.[3] In 1955 a questionnaire was sent out to ascertain what had happened to the individual trainee and the present status of anaesthesiology in his country. Of the 90 trainees who attended the first four courses, 50 are now heads of anaesthesia departments, 12 are whole-time anaesthetists and 7 more are part-time anaesthetists. Seven of the remainder are taking advanced training in anaesthesiology or doing research abroad, while 12 are no longer working as anaesthetists. The study is being pursued in greater detail.

It is interesting to examine the development that has taken place in Denmark itself since the centre was established. In 1949 there was only one chief anaesthetist in the

[3] There were 91 from Denmark, 10 each from Austria and Norway and 7 each from Germany and Yugoslavia. Switzerland sent 6, Finland and Spain 5 each, and Greece, Italy, Portuguese territories, and Sweden each sent 4. The remaining 17 countries sent either 1 or 2 trainees. The trainees attending this year's course include 1 from the USSR and 1 from Poland.

whole of Denmark; now there are 34, and 28 of these have been trained at the centre. Ten of the 28 subsequently had additional training in the USA or Great Britain. In 1954, university chairs in anaesthesiology were established in Copenhagen and Aarhus. It is also worth mentioning that during the period 1950 to 1957 four of the Danish instructors were sent abroad as medical consultants by WHO. The scene has thus undergone a striking change since the centre was first opened, and there can be no doubt that, as far as Denmark is concerned, the time-lag that normally occurs before the importance of a new specialty is recognized has been greatly reduced. It is also known that there has been a steady increase in the number of departments of anaesthesia in many other countries and that post-graduate training is being carried out by former trainees in Norway, Spain, Yugoslavia and Taiwan. It cannot be taken for granted, however, that these results have been due entirely to the influence of the centre.

Some criticisms

On the questionnaire sent out to trainees, criticisms of the course were also invited. Some of the suggestions received have already been taken into account in the planning of subsequent courses. On the administrative side, several trainees complained of the lack of homogeneity of the group taking the course, a difficulty already referred to. This in turn was reflected in the variety of criticisms made concerning technical aspects. Thus, some trainees complained that there was no obstetrical anaesthesia, others that there was no paediatric anaesthesia. Again, some would have welcomed more attention to thoracic anaesthesia, others to regional anaesthesia, while some trainees complained of the neglect of such subjects as hypothermia, controlled hypotension, and the use of an extracorporeal circulation. With a course of only 12 months' duration and the present method of selecting trainees mainly from countries entitled to receive technical assistance, it is clearly impossible to meet all the widely differing requirements of the individual trainee. Consideration has therefore been given to the possibility of increasing the length of the course to 18 months or 2 years and of demanding from applicants for admission a higher standard of previous training and experience. The aim would then be to turn out fully qualified anaesthetists at the end of the course.

Keeping in touch

Perhaps the most important feature of the whole project is the fact that at least 250 physicians interested in anaesthesiology —trainees, instructors and consultants— have at one time or another been in contact with each other and with WHO. This contact is being maintained, partly by direct correspondence between individuals but also by means of a newsletter, *Anaesthesia News Copenhagen*, which is sent four times a year to all those who have taken part in the courses. To strengthen the contacts still further and to provide a follow-up to the Copenhagen courses, WHO is arranging a seminar on recent advances in anaesthesiology to take place somewhere in Europe in 1959. A number of former trainees will be invited to attend this advanced course.

Russian translation of WHO monograph on poliomyelitis

A Russian translation of the monograph *Poliomyelitis* (*World Health Organization: Monograph Series*, No. 26) was published in 1957 by the State Medical Literature Publishing House, Moscow. The translation is by B. I. Kaplan-Dibobes and M. K. Voroshilova. This monograph was originally published by WHO in English and French in 1955, and a Spanish version in now in preparation.

PROGRESS IN MALARIA ERADICATION IN TAIWAN

The figures speak for themselves: in 1951 there were about 1.2 million malaria cases in Taiwan; in 1956 the number of confirmed cases was exactly 492. This result, obtained after five years of intensive control, indicates that malaria may well be completely eradicated in Taiwan within three to five years, if nothing happens to change the epidemiological situation.

What are the reasons for this remarkable success? The question is not without importance for the many other countries engaged in malaria eradication. It is true that Taiwan has had the benefit of a particularly favourable combination of circumstances — for example, its insular position and very dense population—but the achievement is none the less a very real one. The pages that follow give an account[1] of the methods —some of them new—which were employed in the Taiwan campaign, and of the difficulties which had to be overcome or still remain.

Control programme and eradication programme

When, in 1951, the Taiwan Provincial Government decided to undertake malaria control throughout the island, this decision was justified for several reasons: the country had a sufficient number of public health personnel, the results of operations carried out from 1946 to 1949 had been encouraging, the necessary insecticides could be largely made in the country itself and, finally, approaches to international and bilateral assistance organizations had brought offers of technical and material aid.

The aim of the initial project, as defined in the agreement between the Chinese Government and WHO, was to reduce the incidence of malaria in four years, from 1952 to 1955, to such an extent that the disease would no longer represent a major public health problem. Towards the end of 1955, however, the encouraging results led to the conversion of the malaria control programme into an eradication programme. Thus there was no break in continuity between the two programmes, carried out jointly by the Taiwan Provincial Malaria Research Institute (TAMRI)—the successor of the Taiwan Malaria Institute, set up in 1946 by the Rockefeller Foundation—and by WHO, with the assistance of the International Co-operation Administration (ICA), the Council for United States Aid (CUSA) and the Joint Commission on Rural Reconstruction (JCRR).

Before we go on to consider the various features of the programme, it may be helpful to give some background information concerning the country, the structure of its health services and the malaria situation in 1951.

The setting of the campaign

The province of Taiwan, which includes the large island of Taiwan (formerly known as Formosa), two-thirds of which is mountainous, and several small neighbouring islands, has an area of 13 886 square miles. The climate, which is tropical or sub-tropical, is characterized by an average annual temperature of 74°F and an average annual rainfall of 50-250 inches, according to the region. The population (more than 9 000 000 in 1956) is concentrated in the western coastal plains, at the foot of the western slopes of the central mountain chain, and in some strips along the eastern coast. The western plains have a good road system.

Every large administrative division (five municipalities, sixteen hsiens and one special administrative district) has a health centre. The smallest administrative unit (the township or city district) is served by a health station. The island has, in all, 22 health

[1] Based on a report on malaria control and eradication in Taiwan (May 1952 to June 1957) prepared by the Taiwan Provincial Malaria Research Institute (TAMRI) and the WHO Malaria Team in Taiwan. A shortened version of this report will appear in the *Bulletin of the World Health Organization*.

centres and 368 health stations, which act as headquarters for various health projects, including malaria eradication. Malaria control was, in fact, the first project conducted on an island-wide scale whose services were integrated with those of the local health stations.

Endemicity situation in 1951

During the war the malaria treatment stations set up by the Japanese ceased to function and malaria spread unchecked. There are no figures showing the extent of the 1942-1945 epidemic. However, malariometric surveys carried out in 1946 indicated parasite rates of 20-40% among sample groups of children in the primary schools.

The endemicity situation was as follows at the outset of the operations: hyperendemic regions in the foothills and in the mountains up to a height of 1000 metres; hypoendemic regions at altitudes of over 1000 metres, in the municipal centres, the south-western coastal area and the adjacent islands; mesoendemic regions in the rest of the territory.

Measurement of malaria

In order to study malaria epidemiology, define the areas to be sprayed, assess the progress made after each annual spraying campaign and track down remaining foci of transmission in the treated areas, a certain number of parasitological survey techniques were developed. These called for extremely thorough standardization and co-ordination. We shall deal here, in particular, with those used in surveys covering the whole territory.

Parasite density

On a fixed date — 17 December — every year since 1952, 150 local malaria technicians have each taken blood samples from 100 pre-school-age children living in the most malarious of the villages served by their health stations. These samples — averaging from 14 000 to 15 000 — are immediately sent to the headquarters laboratory, where more than 100 microscope fields of each thick smear are examined in about three minutes. The average parasite rate thus determined for this age-group fell from 9.74% in 1952 to 4.50% in 1953 after the first spraying campaign, then to 1.18% (1954), 0.20% (1955), and 0.01% (1956).

From December 1954 to May 1955 another survey, this time covering infants, was carried out to determine whether new infections had occurred after two DDT treatments. Out of the total of 63 460 smears examined only 8 were found positive, 5 being infected with *falciparum* and 3 with *vivax*.

Spleen enlargement

Several national spleen surveys have been carried out in all the primary schools of the island, except in the centres of the large towns, using the Hackett technique, as modified by Chen, Wu & Hsieh. In the first survey, in 1952, sample groups of 50 schoolchildren from the most malarious village in each township were examined. In the course of the second and most extensive survey, in 1953, all the primary schools of the island were visited by WHO and TAMRI malariologists. In each school, a group of 200 children from the elementary classes underwent a spleen examination; 147 089 samples were prepared and examined. The 1955 survey was restricted to one school per township, namely the one which had previously given the highest spleen rate. The average spleen rate for the whole island, obtained in these surveys, was 25.52% in 1953, with an average enlarged spleen of 1.66, and 11.71% in 1955, with an average enlarged spleen of 1.29.

General morbidity

In order to collect other epidemiological data, house-to-house fever-case surveys were also carried out after each spraying campaign in regions which had formerly been very malarious. Such surveys constitute the principal means of detecting residual cases, as we shall see later on.

Study of the vectors

Continuing, after the war, work commenced by Japanese entomologists, research workers

such as Chow, Watson, Chang, Tseng, Hsieh and Pletsch, have dissected a total of nearly 100 000 specimens of the various species suspected of playing some part in malaria transmission in Taiwan. Thanks to their patient investigations, it was concluded that the main vector was *A. minimus minimus*, one of the most widespread mosquitos, particularly in the hill areas and in well-irrigated districts. Study of the habits of this anopheline showed that it is very anthropophilic. In the daytime it is found in dwellings, where it settles preferably under beds or other furniture, as well as on ceilings and walls up to a metre from the floor. All this information was of great value to the engineers who developed the spraying technique.

So as to determine the effect of spraying and to detect any subsequent signs of insecticide resistance, a certain number of collecting stations—ordinary dwelling houses—were visited once or twice monthly throughout the duration of the operations. Other untreated places (cattle sheds, larval breeding places) were also regularly examined. Large periodical collections of adults and larvae at other sites in the island confirmed the information obtained by the collecting station system, namely that the anopheline species had generally disappeared from dwellings after the first DDT spraying.

In certain areas, *A. minimus minimus* was even eradicated. Such an achievement is sufficiently uncommon to be worth special mention. However, it seems that this anopheline can maintain colonies in isolated areas of the bush without having access to human blood. So far there is no proof of the appearance of acquired resistance, either behavioural or physiological, in the case of *A. minimus minimus*. It is believed that other anophelines, particularly *A. maculatus*, may be responsible for the persistence of transmission in certain foci.

Insecticide spraying

The extent of the areas to be sprayed every year is based on the spleen rates of schoolchildren (35% or more in 1953; 10% or more in 1954). The spraying programme also covered townships with lower rates than these, when they were surrounded by other townships requiring treatment.

The population protected by spraying was 1 526 000 in 1953, 5 467 664 in 1954, 5 640 325 in 1955 and nearly 7 000 000—i.e., the whole population of Taiwan, apart from the centres of the large towns—in 1956.

Plan of operations

Once the area to be sprayed was defined, it was divided into four regions, to be treated one after the other. The headquarters engineering service then drew up the plan of operations (amount of insecticide, number of sprayers, vehicles, local cost of operations, number and training of personnel, etc.). This plan was published in the *Provincial Gazette* a year before its application, in order to inform the local administrations in advance of the number of employees they would have to supply and the anticipated cost. The date and place of the training course were notified by circular letter to the administrations of the hsiens and municipalities two months before the commencement of operations.

At the beginning of each annual spraying period, a special training course was organized at the campaign headquarters for the 28 to 35 supervisors responsible for the programme in the hsiens and municipalities. These supervisors subsequently directed regional training courses for those in charge of spraying in the townships. The latter in turn trained local sprayers and workers. At the end of this training period, which lasted about a month, spraying was commenced.

Operations commenced on the same day in all the townships of a given region. The visit of the team was notified to all the village headmen and in many cases the local press published articles on the malaria control campaign. On an average, one spraying team treated the dwellings of 7000 persons in 60 working days.

Insecticides used

Throughout the control campaign an effective annual dose of 2 g/m² of technical DDT was used, applied in the form of 75%

DDT water-dispersible powder. Since 1956, this has been replaced by a DDT-BHC mixture in a dose of 17 mg of BHC gamma isomer and 2 g of technical DDT per square metre. At the outset, all the DDT was imported from the United States. In 1953, a national factory commenced manufacture and supplied one-third of the insecticide required in 1953, half in 1954, four-fifths in 1955 and the total amount in 1956.

As regards equipment, it may be mentioned that a factory in Taipeh has produced an excellent compression sprayer as well as a multi-outlet pump.

Difficulties encountered

In 1955, spraying teams were refused admittance to a number of houses; as a result, the dwellings of 3.7% of the population to be protected could not be treated. Many reasons were given for these refusals—ineffectiveness of DDT against insect pests, damage to silkworm- and fish-breeding, stains on walls and furniture. A study of the mortality caused among silkworms and "fish-seedlings" made it possible to deal with one of these causes of complaint. Another was tackled in 1956 by the decision to use a mixture of DDT and BHC, which, to the general satisfaction, killed a high proportion of insect pests.

A further difficulty is the increasing reluctance of the municipal mayors and councillors to provide funds for malaria control, as it is hard for them to realize that it costs as much to eradicate the few remaining cases of malaria as it formerly did to combat generalized malaria. So far, however, thanks to local public health personnel, the programme has been effectively continued.

Surveillance stage

The initial surveillance operations date back to December 1954. When it was decided to attempt to eradicate malaria, a complete surveillance system was organized, including not only the detection, study and elimination of residual foci of transmission but also the detection and treatment of residual cases of infection.

Any area where transmission and residual cases of infection are still found after DDT treatment is regarded as a residual focus of transmission. The residual cases of infection are divided into three categories: (1) infection among children born after the initial spraying campaign; (2) *falciparum* infections (excluding infections in group (1)); (3) *vivax* and *malariae* infections (excluding infections in group (1)). Most persons carrying parasites are found among adult fever cases (0.26% in 1956). From December 1954 to June 1957, out of 78 618 infants and children born after the commencement of the first spraying campaign, only 19 gave positive blood tests.

At present it is estimated that various types of indigenous malaria are still prevalent in 84 townships, with a total population of more than 1.2 million. A fifth of this population is under strict surveillance.

A body of technicians well trained in surveillance methods—preparation of blood smears, microscopic examination, treatment of malaria sufferers—has been stationed at strategic points in all the regions under surveillance. Each technician is allowed three months in which to tour an area with 5000 to 6000 inhabitants, visiting private persons, hospital establishments, factories, plantations, etc.

The details given by public health officers or private practitioners represent what is termed "passive case-finding". Since July 1955, notification of malaria cases has been compulsory and treatment is free. However, probably owing to lack of proper information, physicians have not collaborated to the extent expected.

In order to eliminate foci of transmission, recourse is had to emergency spraying and to the mass treatment of the whole population of the focus. The treatment schedule so far employed—a single dose of amodiaquine or chloroquine (10 mg or 12 mg, respectively, per kg of body weight)—has certainly led to a great reduction in the parasite rate (from 6% to 0.66% in certain villages), but it is hoped to obtain still better results in years to come by the regular administration of these drugs, and by also administering a dose of 15 mg of primaquine per day for two weeks in cases of *vivax* or *malariae* infection.

General organization of the programme

At the outset, in accordance with the agreement reached with WHO, the technical and general direction of the operations was assumed by the WHO Senior Malaria Adviser, on behalf of the Chinese Government. The Regional Director of WHO for the Western Pacific and the Regional Malaria Adviser gave technical advice. However, the responsibility for directing operations was gradually transferred to the TAMRI personnel and by 1955 this transfer was complete. From then onwards, the members of the WHO team acted solely as consultants. It was also in 1955 that the two malaria control programmes—military and civil—were amalgamated. As far as possible, the campaign headquarters has retained control of everything connected with general planning and programme assessment, gradually allowing the health centre personnel to take over the direction of local operations.

At first sight it would seem that a programme on this scale must have called for—and would still need—a very large staff. This is by no means the case. In June 1957, TAMRI employed 77 agents, including 6 malariologists, 3 entomologists, and 22 parasitological and entomological technicians. These are the only persons working for the project full-time. Apart from sprayers and workmen recruited by the townships on a temporary basis, the rest of the personnel required consists of physicians, health engineers and other workers in the public health centres and stations who are assigned to malaria control work for two months every year.

From May 1952 to the end of 1956, more than US $5 000 000 were expended—including $4 000 000 for control operations—or rather more than $0.50 per inhabitant.

The contribution of the Chinese Government (about US $2 300 000) has served to cover wages, transport costs, cost of equipment and supplies purchased in the country and all maintenance expenses. American funds (about US $2 600 000) have been used primarily for the purchase of DDT and sprayers, as well as for wages and transport costs. The salaries and travel expenses of the WHO experts have been paid by the Organization; the technical documentation and part of the equipment not available in the country have been supplied by WHO, using United Nations Technical Assistance funds (in all, US $174 000).

Continuation of the eradication campaign

Even if the antimalaria programme were to end now, the efforts of the past seven years would not have been in vain, for many lives have been saved and the national economy has been considerably strengthened as a result. Nevertheless, one must be realistic. The present low endemicity represents an epidemic potential and serious outbreaks could occur in a year or two. For this reason epidemiological work should be continued with unremitting energy so as to determine what factors help to maintain transmission (other vector species, natural and acquired anopheline resistance to insecticides, seasonal movements of the population, faulty spraying, primitive housing conditions, etc.).

In 1958 the spraying programme will protect some 400 000 inhabitants; it will cover all the residual foci of transmission discovered in the last two years and all former hyperendemic regions which still have a population of *A. minimus minimus* and where transmission seems to persist. After 1958, systematic spraying will cease, except locally in emergency cases. From then onwards it will, in fact, be more economical to employ medicinal treatment for the few remaining cases of malaria.

The success of the last phase of surveillance will depend in the final analysis on the inhabitants themselves, for it is to be feared that they will see less and less reason for opening their doors to sprayers and investigators and submitting to the necessary examinations. They can hardly be blamed for this, but an additional effort to enlighten them is essential and the Taiwan public health personnel should certainly be able to undertake this task.

EXPERIMENTS WITH FREEZE-DRIED BCG VACCINE

Liquid BCG vaccine is sensitive to heat and must be kept at a temperature of 2-4°C during storage and transport if it is to be prevented from losing its potency. This requirement creates serious problems in large-scale BCG vaccination programmes such as those carried out under the auspices of WHO and UNICEF in tropical countries and in regions where communications are slow and difficult.

Assessment of the results of mass vaccination campaigns has shown that the degree of allergy provoked by BCG is not always up to the desired level, and on occasions may be quite low. One of the reasons for this is believed to be failure to keep the vaccine at the proper temperature during storage and transport.

In Japan, workers have for a long time been experimenting with freeze-dried BCG vaccine in an endeavour to increase the stability at higher temperatures. Several papers on this subject have been published in the WHO Bulletin and Y. Obayashi has written a monograph describing exhaustive studies on freeze-dried BCG vaccine.[1]

Recently, the effects of incorporating certain adjuvants in the vaccine to improve its heat-stability have been examined.

The addition of 1-2% sodium glutamate, for example, has given promising results and the product appears to be remarkably stable to heat.

At first, freeze-dried vaccines were used only on a limited scale and in national projects, but in view of the needs of the WHO/UNICEF mass vaccination campaigns, the WHO Tuberculosis Research Office (TRO) decided to study the possibilities of using freeze-dried BCG vaccine with sodium glutamate as adjuvant on the international level. The results of the first of these studies are reported in a recent number of the WHO Bulletin.[2]

A series of field trials with this product was commenced in April 1956 with the vaccination of schoolchildren in Ilorin (Nigeria). Two freeze-dried vaccines were used —one with 1% sodium glutamate and the other with 2% sodium glutamate as adjuvant. The vaccines were stored for 15-16 months at 2-4°C, and thereafter some ampoules of each were kept for one month at temperatures of (*a*) 20°C during the day and 37°C during the night (to simulate the oscillations of temperature observed in certain tropical regions); (*b*) 37°C; or (*c*) 42°C. For the purpose of comparison, fresh, liquid vaccine was used, injected 13-15 days from the date of preparation after having been kept at a temperature of 2-4°C.

Before vaccination, the tuberculin test was applied to determine which of the children showed tuberculin sensitivity (5 TU injected intradermally into the dorsal surface of the left forearm). Vaccination was then performed on the 368 children who did not react to the test or who reacted with a local induration of less than 10 mm transverse diameter. 0.1 ml of reconstituted freeze-dried vaccine, equivalent to 0.05 mg of bacilli (moist weight), or 0.1 ml of fresh, liquid vaccine, equivalent to 0.075 mg of bacilli (moist weight), was injected intradermally into the left deltoid region. The vaccines were used in rotation.

Six months after vaccination, the tuberculin test was again applied (5 TU in a volume of 0.1 ml administered intradermally) to determine the level of the allergy produced by the vaccine. The tests were read three days after injection of the tuberculin, the transverse diameter of the palpable induration being measured.

Two important findings were: (*a*) the freeze-dried vaccine to which sodium glutamate had been added and which had been stored for 15-16 months at 2-4°C produced the same level of allergy as did fresh liquid vaccine, and (*b*) 30 days' exposure of freeze-dried vaccine to temperatures of 20°-37°C, 37°C and 42°C caused only a very slight loss of allergenic potency. The lesion-producing

[1] *World Health Organization: Monograph Series*, No. 28

[2] *Bull. Wld Hlth Org.*, 1957, 17, 289

capacity of the freeze-dried vaccine was found to show a similar trend to the allergenic potency, a slight reduction in the mean size of the lesions being observed with vaccines stored at the highest temperatures.

On the basis of these findings, it may be affirmed that freeze-dried vaccine stabilized with sodium glutamate, as used in this study, is remarkably heat-resistant. Unlike the liquid vaccine, it suffers no significant loss of allergenic potency even after 30 days' exposure to tropical temperatures.

The level of allergy was determined six months after vaccination, and it remains to be seen whether the level will be maintained over a longer period.

A start has recently been made with the industrial production of freeze-dried vaccine, stabilized with sodium glutamate. If the long-term results are as good as those obtained so far, an important step will have been taken towards the solution of a major technical problem connected with mass BCG vaccination.

REACTIONS FOLLOWING VACCINATION AGAINST PERTUSSIS

The effectiveness of pertussis vaccination has now been amply proved, but, unfortunately, the procedure is not completely free from risk. This is a drawback that applies, however, to several other types of vaccination, e.g. against smallpox, yellow fever, rabies and typhoid. What are the risks involved in pertussis vaccination and to what extent are they outweighed by the undoubted advantages of this method? This question is answered by Dr W. C. Cockburn, in an article which will shortly appear in the *Bulletin of the World Health Organization* and is summarized below.

Reactions

Tenderness at the site of injection, inflammation, swelling and fever are sometimes seen following pertussis vaccination. These reactions remain mild when the vaccine, either alone or associated with toxoids, does not contain alum. It appears that this substance, which is present in certain vaccinal preparations, aggravates the reactions and leads to more frequent formation of sterile abscesses. Alum does not augment the protective power of pertussis vaccine; consequently its addition to the plain vaccine is unnecessary. Neither is its use justified in mixed vaccine preparations containing pertussis vaccine, since the latter itself acts as synergist with respect to the toxoids in the mixture. The route of injection and the volume inoculated also influence the severity of the reactions. In general, intramuscular injection is better tolerated than subcutaneous injection.

Sequelae

Occasionally, injections of pertussis vaccine have been followed by more serious and lasting complications of a neurological nature. Although all encephalopathies occurring after pertussis vaccination cannot be attributed to the vaccine, authentic cases have been reported during the last 20 years. These have included convulsions and sometimes hemiplegia or other permanent brain lesions. The pathogenesis of these encephalopathies is still unknown, but it seems to differ from that of cases associated with other forms of vaccination.

The risks are extremely small, however, when it is remembered that only a hundred or so cases have been described in the literature for all the hundreds of millions of vaccinations carried out. It should be borne in mind that children may suffer from serious cerebral disorders during the course of most infectious diseases, including infections of the respiratory tract, and that, long before the use of pertussis vaccine, acute cerebral paralysis of childhood had been described, with symptoms closely resembling those of post-vaccinal accidents. The significance of such accidents must therefore be interpreted with great care, particularly if

they occur several days or even weeks after vaccination. According to published reports, it would seem that accidents attributable to pertussis vaccine generally occur within the 72 hours following the injection.

During vaccination campaigns carried out in England in recent years, two groups, totalling 30 000 children, were followed up with special care for three years after vaccination. No serious neurological sequelae were seen, although there were cases of convulsion without permanent injury which could not be definitely attributed to vaccination. During these trials, care was taken not to vaccinate any child with a history of convulsions, epilepsy, mental deficiency, encephalitis or other similar complaints. This precaution was taken on an empirical basis, for there is no proof that such a history creates conditions favouring the appearance of neurological sequelae. The decision seems a wise one, however, although paediatricians agree that vaccination involves less risk for children suffering from convulsive disorders than does pertussis itself. As a further precaution, no child was vaccinated less than one month after measles, mumps, influenza or vaccination against smallpox.

Another serious complication, first reported in 1950, is the provocation of an attack of poliomyelitis, sometimes with paralysis of the limb in which the injection has been made. A special study of this question carried out under the auspices of the Medical Research Council of Great Britain led to the conclusion that the injection of pertussis vaccine, either alone or admixed with plain toxoids or toxoids to which alum has been added, carries a definite risk. This risk has been found to be greatest in the case of mixed antigens to which alum has been added. The frequency of paralysis during the total period of these studies is estimated to be as follows: 1 case in every 15 000 injections of mixed antigens with the addition of alum; 1 case in every 20 000 injections of mixed antigens without the addition of alum; 1 case in every 170 000 injections of plain pertussis vaccine.

These figures give an approximate idea of the extent of the risk, which will remain a source of anxiety until it is known whether poliomyelitis vaccination gives protection against accidents of this nature.

The report of the Medical Research Council revealed an unexpected fact. It seems that the risk of induced poliomyelitis is at least as high in the three months preceding the "epidemic" poliomyelitis period as during that period itself. Consequently, pertussis vaccination campaigns should be intensified during the winter. But vaccination cannot be limited to this season alone, for it is essential to be able to vaccinate infants at any time, as pertussis is particularly dangerous during the first months of life.

Assessment of the risks

The risks of pertussis vaccination can only be rightly assessed in relation to those of the disease itself. Pertussis is a serious disease and the chances of a fatal outcome or the development of grave neurological or respiratory complications are by no means negligible. In 1951, a study by the Medical Research Council put the proportion of complications occurring in an unvaccinated control group of children at 4% (calculated on 687 cases). The same study reported that 60% of the children had suffered from paroxysmal coughing for eight weeks or more. The risks attendant on vaccination are very much smaller and there can be no doubt that it should be generally adopted so as to reduce the incidence of the disease. In addition, precise information on post-vaccinal accidents should be obtained from all countries, and research should be continued on the pathogenesis of encephalopathy and on the development of a safer vaccine.

EXOPHILY IN ANOPHELINES AND MALARIA CONTROL

The exophily shown by anophelines—i.e., the tendency of these mosquitos to rest outside in the daytime rather than in man-made shelters—may help to maintain a certain reservoir of malaria infection (residual malaria) in regions where a well-organized campaign employing residual insecticides would otherwise be expected to eradicate the disease.

In Africa in particular, the exophily of *A. gambiae*, one of the chief malaria vectors and one of the species of *Anopheles* showing the greatest biological variations, is a factor that must be taken into consideration in organizing control measures. Two authors have recently dealt with this question in the *Bulletin of the World Health Organization*. Gillies [1] has discussed in detail the problem of exophily in *A. gambiae*, on the basis of studies made in Tanganyika. He considers in turn the different forms of exophily as classified by Senior-White. These are: obligatory exophily, when there are no houses in the area inhabited by the mosquito, as happens in the case of *A. culicifacies*, in the uninhabited jungle of Ceylon; facultative exophily, when there are numerous houses and shelters but one of the preferred hosts is to be found outside; deliberate exophily, when the mosquito either bites indoors but leaves before daylight (*endophagic*)—as in the case of *A. maculatus* in Malaya—or bites out of doors and avoids resting-sites in houses (*exophagic*), e.g., *A. coustani* and *A. pharoensis*. The stage of gonotrophic development of the females—unfed, gorged with blood or gravid—is also of significance in connexion with exophily.

What is the role of exophily in the maintenance of endemic malaria when residual insecticides are used for systematic house-spraying? As regards *A. gambiae* in Africa, Gillies concludes that at present it is impossible to state with confidence that transmission will be completely interrupted by insecticide spraying, regardless of local conditions or the degree of endemicity. It will not be possible to be certain of this until the behaviour of the exophilic groups and the influence of insecticides on them have been accurately determined. If their importance is underestimated, there is a risk that low-grade transmission will be maintained, and that this might be wrongly attributed to a change in the behaviour of the mosquito or in the response of the species to insecticides.

The article by Gillies prompted J. Sautet [2] to point out that exophily was studied long before the use of residual insecticides for malaria control. In the Lebanon, in 1934, exophily was detected among populations of *A. sacharovi* and *A. sergenti* found in caves, holes in walls, or in fields. Similarly, in Corsica in 1935 *A. maculipennis labranchiae* was observed to exhibit exophilic tendencies, varying with the season or the strength of the wind. In the Sudan, research on the exophilic nature of *A. gambiae* has confirmed the possibility of "open-air malaria". Female anophelines, gorged with blood, were found in precarious resting-places, such as holes in silk-cotton trees (Bombax) and fissures in bark. These mosquitos became aggressive at nightfall and were distinctly anthropophilic. In Mauritania, outdoor resting-places of *A. gambiae* have been found in deep holes. Numerous malaria control campaigns have not succeeded in destroying the exophilic group—whether anthropophilic or zoophilic—of the *A. gambiae* population in the islands of Mauritius, Réunion and Madagascar. Referring to his own investigations and those of his co-workers, Sautet states that they have found exophily wherever they looked for it, particularly among species regarded as domestic.

[1] Gillies, M. T. (1956) *Bull. Wld Hlth Org.*, 15, 437

[2] Sautet, J. (1957) *Bull. Wld Hlth Org.*, 17, 367

It has been suggested that exophily, endophily and anthropophily are fixed characteristics, associated with certain races. This question is of great practical importance, but it has not yet been possible to find a definite answer, owing to the absence of genetic data and frequently also of accurate statistical data on the various anopheline species before eradication measures were instituted.

Certain authors have suggested that a change in biological behaviour has occurred in the mosquitos, causing them to avoid and flee from premises treated with residual insecticides. Such centrifugal migrations would explain, at least partially, the exophily of anophelines in treated areas. This theory is not accepted by other workers, however. Sautet, in particular, while not denying the possibility of such an explanation, feels that the problem cannot be settled without a thorough study of anopheline resting- or breeding-places before and after spraying campaigns and over a period of several years, since the anopheline density varies from year to year, both indoors and outside. Sautet warns against errors arising from hasty observations. A short initial survey often indicates the presence of large numbers of anophelines in a malaria zone and the relatively small number of insects found at the circumference of this area is dismissed as negligible. Next comes malaria control, leading to almost complete disappearance of the anophelines. By comparison, the mosquitos in the peripheral area are now considered very abundant. From this it is only too easy to conclude that a migration has taken place, particularly if the new survey is made by a different observer without access to precise figures on the initial situation.

TWENTY-FIRST SESSION OF THE EXECUTIVE BOARD

The Executive Board of WHO held its twenty-first session from 14 to 28 January 1958, in Geneva. The Chairman at this session was Sir John Charles, Chief Medical Officer, Ministry of Health, London, and the Vice-Chairmen were Dr Dia E. El-Chatti, Director of International Health Affairs, Ministry of Health and Public Assistance, Damascus, and Dr P. E. Moore, Director of Indian and Northern Health Services, Department of National Health and Welfare, Ottawa. Dr Hafez Amin, Under-Secretary of State, Ministry of Public Health, Cairo, and Dr A. da Silva Travassos, Director-General of Health, Ministry of the Interior, Lisbon, were appointed Rapporteurs.

At the opening meeting, tribute was paid to two members who had died since the last session. They were Dr J. Zozaya and Dr F. Koch, the members designated by Mexico and by the Federal Republic of Germany. The Chairman welcomed the two members who had been designated to replace them, Dr C. Díaz-Coller and Dr A. Habernoll. He also extended a welcome to Dr L. E. Jaramillo, the member recently designated by Ecuador.

Programme and budget for 1959

One of the principal tasks before the Board was the examination of the Director-General's proposed programme of activities and budget estimates for 1959. After a detailed discussion of these proposals, the Board endorsed the Director-General's effective working budget of $14 287 600. This compares with $13 566 000 for 1958, an increase of 5.3%. More than 80% of this increase is accounted for by an expansion of field activities. Several members of the Board laid emphasis on the desirability of strengthening the technical services at Headquarters, and it was suggested that, in preparing the budget for 1960, a greater percentage of the total expenditure should be set aside for this purpose. With regard to the estimates of expenditure under the United Nations Ex-

panded Programme of Technical Assistance, the Board noted that the funds expected to be provided for Category I projects in 1959 totalled $4 238 000.

Malaria eradication

In pursuance of WHO's policy of securing, as rapidly as possible, the complete eradication of malaria from the world, the Director-General has now drawn up a detailed programme covering the operations planned for the next five years.[1] To ensure that the carrying out of the programme does not prejudice other activities, the Director-General has established a Malaria Eradication Special Account, supplementary to the regular budget and Technical Assistance funds. The total resources available in the account at present are $5 112 000, of which $5 000 000 have been contributed by the United States of America. As the estimated expenditure for 1958 alone is $5 058 000, some concern was expressed by members of the Board regarding the financing of the programme during succeeding years. Dr Hyde (United States of America) stated that the United States intended to make substantial contributions over the next four years, and the Director-General informed the Board that he had already started negotiations with several countries in the hope of obtaining additional funds. It was also possible that contributions might be forthcoming from a number of private organizations, from individuals and from manufacturing firms.

Several members stressed the fact that an appeal for funds would have little chance of success unless it were preceded by a publicity campaign to acquaint the general public with the extent of the malaria problem and with the details of WHO's eradication programme. The Director-General said that, in this context, it should not be forgotten that the eradication of malaria would have important repercussions on economic development. In fact, the concept was based on the belief that eradication would open the way to economic advance, leaving health administrations free to tackle other outstanding health problems. The Board expressed the hope that governments able to do so would make voluntary contributions to the Special Account, and requested the Director-General to take the necessary steps — including adequate publicity — to obtain additional funds, whether from governmental or from private sources.

The concept of malaria eradication is already making good headway in the various regions. In the Americas, it has been agreed that malaria is the most important problem facing the Region, and definite plans have now been drawn up for all except two of the countries. It is estimated that completion of the eradication programme in this Region will cost altogether $145 000 000, of which $100-105 million will be met by the governments of the countries concerned, while a further $20 000 000 is expected to be borne by UNICEF. In the Eastern Mediterranean Region, malaria eradication programmes are already in operation in four countries and are planned for seven others. A special malaria eradication unit is to be established to co-ordinate and supervise the work. Most of the countries of South-East Asia and a number of those in the Western Pacific Region have also adopted eradication as their objective, and an eradication plan is being prepared for the south-eastern part of Africa. Altogether 76 countries have already instituted or are planning to institute eradication programmes; in nine of these eradication has been practically achieved and in seven more it is very far advanced.

Reports from the regions

The Board reviewed the reports of the various regional committees on the sessions held last September. These sessions have already been described briefly in preceding numbers of the Chronicle.[2] The Board showed interest in the progress that has been made in the campaigns against smallpox. In the Western Pacific Region, practically no outbreaks have been reported during the

[1] A special article on WHO's malaria eradication programme will be published in a forthcoming number of the Chronicle.

[2] *Chron. Wld Hlth Org.*, 1957, 11, 351, 381

past four years, and for several years no cases have been confirmed in North or Central America or the West Indies. An improvement in the situation has also taken place in Africa. In South-East Asia, however, there was a rise in the incidence of smallpox in 1957. It was pointed out that, in this Region, the number of cases can be expected to fluctuate for many years to come, until medical services can be extended to cover the vast rural areas.

The Regional Committee for the Americas reported that although the eradication of *Aëdes aegypti* is not yet complete, no outbreaks of yellow fever transmitted by this vector occurred in urban districts during 1957. Outbreaks of jungle yellow fever — transmitted by species of *Haemagogus* — occurred in six countries, however, and another of the periodic waves of the disease began to spread southwards from the Amazon valley.

In this Region, the decline in tuberculosis has been spectacular. In the United States, mortality is now around 8.5 per 100 000 (1956), compared with 26.3 per 100 000 in 1949, i.e., a drop of 68%, while in Chile mortality has fallen by 69% from 201 per 100 000 in 1949 to about 63 per 100 000 in 1956.

Proposal to include sports medicine in the programme of WHO

The Governments of Denmark, Finland, Norway and Sweden had submitted to the Board a formal proposal that " sports medicine " should be included in the programme of WHO. A similar proposal had been made by Bulgaria at the First World Health Assembly in 1948. Scientific information on physical training had subsequently been collected from various sources and submitted to the Third World Health Assembly, which had decided to postpone further action. In support of the present proposal, it was pointed out that outdoor games and athletics are now practised in schools throughout the world and the interest in sport is retained in later life. Sport, it was said, is important both for physical and mental health, and sports medicine is developing into a new specialty. It was thought that WHO might give a lead in stimulating research into the various problems involved and in guiding its application. Several members expressed a desire for a more precise definition of the term " sports medicine " and for a clarification of what the authors of the proposal had in mind; there was some concern lest expenditure on such a project might be prejudicial to other activities. The Board requested the Director-General to examine the proposal further and to submit a preliminary report to the Eleventh World Health Assembly on the kind of programme that might be undertaken by WHO in this new field.

Emergency assistance to Ceylon

Following the severe floods in Ceylon at the end of last year, WHO made available supplies of cholera and TAB vaccine to the value of $11 500. Since then a request had been received from the Government of Ceylon for further supplies, bringing the total cost up to $20 000. The Board approved the action already taken and authorized the Director-General to provide the additional assistance. The Government of Ceylon has stated its intention of reimbursing some, if not all, of the cost of the TAB vaccine.

Other business

A further major task of the Board was the examination of reports from expert committees and study groups. The discussions on these reports are summarized in a separate article below.

The Board had received applications from the International Fertility Association, the International Union of Local Authorities, and the Fédération Internationale de Médecine Sportive, asking to be admitted into official relations with WHO. It was agreed that these Organizations met the requisite criteria and it was therefore decided to accept the applications.

* * *

The Eleventh World Health Assembly will open in Minneapolis, Minnesota, on 28 May 1958, and will be preceded by a special Tenth Anniversary Commemorative Session from 26 to 28 May. The twenty-second session of the Executive Board will also be held in Minneapolis, commencing on 16 June 1958.

REPORTS OF EXPERT GROUPS REVIEWED BY THE EXECUTIVE BOARD

During its twenty-first session, the WHO Executive Board reviewed a number of technical aspects of the Organization's work —reports of expert committees, reports of study groups, conferences, etc. Some of the points that emerged during the discussions are summarized below.

Reports of expert committees

Biological standardization

The eleventh report of the Expert Committee on Biological Standardization, which met in Geneva from 16 to 21 September 1957, deals with problems relating to the international standardization of a large number of antibiotics, hormones, antigens, antibodies and other biological substances. The number of antibiotics for which international standards are available has been brought up to eleven. An international unit for pertussis vaccine is defined and the possibility of standardizing poliomyelitis vaccine and cholera vaccine discussed. The international standardization of smallpox vaccine, rabies vaccine, and swine erysipelas vaccine is in progress. Steps are being taken to establish international reference preparations for three types of poliomyelitis sera, syphilitic human serum, yellow-fever immune serum, antistreptolysin O, and Rhesus blood-typing sera. The Committee decided not to set up international reference preparations for leptospirosis vaccines, since their antigenic composition varies widely in different parts of the world according to the prevalent strain of leptospira. In the discussion of the report by the Executive Board, Professor Canaperia (Italy) said he thought there would be some advantage in having international reference preparations for leptospirosis vaccines that would facilitate evaluation of the antigenic content of other vaccine preparations. On behalf of the Director-General, it was stated in reply that, while this view was correct, the problem had been considered too complex to be tackled at that time by the Committee; this did not mean, however, that the possibility of setting up such reference preparations would not be discussed at some future date.

International Pharmacopoeia

The Board had before it the fifteenth report of the Expert Committee on the International Pharmacopoeia as well as the seventh report of the Sub-Committee on Non-Proprietary Names. It was explained on behalf of the Director-General that the main task of the Sub-Committee, which met from 12 to 15 June 1957, had been to study suggestions for non-proprietary names received from various sources. It had selected 159, and the list would shortly be published in the Chronicle (see page 102 of this issue). The names recommended by the Sub-Committee in previous reports were being increasingly used throughout the world in official publications, and as a result there was less confusion than there had been in the past.

The fifteenth report of the Expert Committee, on the session held from 2 to 8 October 1957, will not be published as the material will be included in the *International Pharmacopoeia*. The main topics that had been discussed were: the monographs to be

included in the supplement to volumes I and II of the *International Pharmacopoeia*; specifications for reagents; problems arising from the rapidly increasing number of new pharmaceutical preparations; the possibility of publishing individual specifications without waiting for the publication of the *International Pharmacopoeia* itself; and questions relating to the second edition of the *International Pharmacopoeia*.

Addiction-producing drugs

The Expert Committee on Addiction-Producing Drugs had submitted its eighth report, following a session held from 14 to 19 October 1957. The Committee noted that governments are becoming more and more interested in technical assistance to combat drug addiction and expected an expansion of WHO activities as a result. The continued increase in the consumption of certain narcotic drugs was thought to be due in part to their wider use in medicine. The Committee recommended that a number of new drugs with morphine-like analgesic and addiction-producing effects be placed under international control and that the control measures already in existence for certain drugs should not be relaxed. Professor Canaperia (Italy) asked what were the criteria employed by the Committee for deciding whether a drug had addiction-producing properties. In the reply, it was stated that the decisions of the Expert Committee were greatly influenced by the results of certain clinical experiments specially designed to test physical dependence on addiction-producing drugs; one of the main centres for performing such tests is at Lexington in the United States of America. There was some discussion regarding substitutes for diacetylmorphine (heroin). The Committee had debated this question at considerable length and decided not to issue a list of substitutes but to leave it to the individual physician to decide what drugs should be used in each case. This decision had been reached partly because a vast amount of literature about morphine-like analgesics is already available.

Water fluoridation

The Expert Committee on Water Fluoridation, which met from 26 to 30 August 1957, considered that the prevention of dental caries could only be tackled on a wide scale by water fluoridation. In the United States of America some thirty million people living in fifteen hundred communities are already benefiting from this measure, and the Committee could find no evidence that water with one part of fluoride per million impairs health. The Committee concluded that the efficacy, safety and feasibility of water fluoridation has been established, though there are still a number of unsolved problems.

The statement in the report that "the effect of fluoride continues into adult life" was criticized by Dr Díaz-Coller (Mexico). It was explained, in reply, that the Committee had considered that fluoridation prevented caries among children and that the effect persists for a considerable period. Dr Díaz-Coller stated that he was anxious to dispel the impression that fluorides had a protective effect on adults. He also thought that more emphasis might have been placed on the fact that the amount of fluoride required is dependent upon climatic factors influencing the amount of water consumed. It was agreed that this was an important point which would undoubtedly be taken into account by public health authorities.

Poliomyelitis

The second report of the Expert Committee on Poliomyelitis, which met from 15 to 20 July 1957, was very well received by the Board and provoked a lengthy discussion. Part of the report deals with the large-scale use of inactivated vaccines and with problems associated with their production. Recommendations are made concerning the organization of vaccination programmes and serological surveys, and a better utilization of regional laboratories collaborating with WHO is advocated. A considerable portion of the report is devoted to the possibility of field trials with live poliomyelitis virus vaccine and the specifications of strains to be used.

The Committee suggested a classification to avoid confusion of poliomyelitis with other diseases; and it recommended further research on inactivated and live virus vaccines, on combinations of other immunizing agents with poliomyelitis antigens, and on improved laboratory procedures.

Professor Pesonen (Finland) praised the report and offered a number of comments. The epidemiological studies advocated by the Committee, though providing the best data for assessing actual needs, required a great deal of work, time and money. He reported a field study recently carried out in Finland and not yet published. The distribution of poliomyelitis antibodies in five communities had been found to be statistically the same in every age-group. He agreed that the term " non-paralytic poliomyelitis " should not be used, particularly during epidemics, as many cases of aseptic meningitis and meningo-encephalitis might easily be so described. The report gave a very valuable account of diseases resembling poliomyelitis and it was important to disseminate that knowledge among workers in the field. He also endorsed the Committee's recommendation that experiments with live attenuated vaccines should be continued, and said it would only be a matter of time before it would be possible to use them on a wider scale. Their administration was technically easier and would meet with less opposition from those who resisted inoculations in principle.

Dr Metcalfe (Australia) said that since 1955 Salk vaccine had been distributed in Australia as rapidly as it could be produced. Up to the present time, every child of school age had received three injections and some states had already started a vaccination programme for adults up to 45 years of age. Last year there had been only 138 cases of poliomyelitis compared with over a thousand cases in previous years. There had been no complaints of reactions and no case of poliomyelitis following injections.

In answer to questions from the Chairman, Sir John Charles (United Kingdom), it was stated that, although there was laboratory evidence that antibodies were produced following intracutaneous inoculation, there was no statistically accepted field evidence of protection comparable to that from the United Kingdom and United States field trials. The Committee had taken the view that the practical results were not yet good enough to allow any margin for reducing the dose by means of intracutaneous inoculation or the use of adjuvants.

Brucellosis

The joint FAO/WHO Expert Committee on Brucellosis met from 7 to 12 October 1957, and subsequently submitted to the Board its third report, which gave an up-to-date account of knowledge of the subject. Particular attention had been paid to *Br. melitensis* infection in sheep and goats, the main source of human infection. This form of brucellosis constitutes a serious economic and public health problem in many countries, and FAO, in collaboration with WHO, has sponsored both laboratory and field work aimed at controlling the infection. Great efforts have been made to develop a suitable vaccine, and FAO and WHO are already making joint plans for carrying out field trials of certain selected vaccines that have shown promise in laboratory experiments.

Professor Canaperia (Italy) asked whether research workers had been able to develop methods for distinguishing between the natural antibodies of the disease and the antibodies produced by the vaccine in animals. In reply, it was stated that certain tests on milk whey serve to give some indication, but no absolutely reliable techniques have yet been developed and research is continuing. In an answer to a further question from Professor Canaperia regarding evidence that vaccination of humans with Strain 19 might have a protective value, it was pointed out that Strain 19 has produced reactions and illness in humans in some instances. A living vaccine indistinguishable from Strain 19 has been widely used in the USSR, where several million persons have been vaccinated, but sufficient first-hand information is not yet available to enable the experts to pass a final judgement. WHO's present policy is to encourage research on a killed vaccine for

possible immunization of humans against brucellosis, and to try to obtain new information on the use of living vaccine for this purpose.

In a statement on behalf of FAO it was pointed out that the satisfactory control of brucellosis is closely connected with the quantity and quality of the milk supply and that FAO and WHO are also working jointly on milk hygiene. Dr Togba (Liberia) asked whether world-side acceptance of pasteurization instead of the grading of milk was imminent. It was stated in the reply that the grading of milk is being used less and less, and that the use of unpasteurized milk has been strongly condemned by the FAO/WHO Expert Committee on Milk Hygiene. The objective of WHO is to encourage the use of heat-treatment (sterilization or pasteurization) as a means of eliminating the transmission of certain diseases through milk.

Nutrition

In introducing the fifth report of the Joint FAO/WHO Expert Committee on Nutrition, which met from 22 to 29 October 1957, it was explained on behalf of the Director-General that this report differed somewhat from the reports of other expert committees because the main function of the Committee was to review past programmes and advise on future planning; since it was first constituted in 1949, it had played an important part in co-ordinating the nutrition programmes of the two organizations. During the period reviewed in the report, meetings of the FAO Committees on Calorie Requirements and on Protein Requirements had taken place. The Joint Committee had agreed that a further revision of the report on calorie requirements was unlikely to be necessary for some time to come, whereas the report on protein requirements—a much more difficult and complicated subject—would probably need revision within a few years because of the rapid progress being made in this field. The studies on protein malnutrition are perhaps the most important of the continuing projects in the nutrition programme of the two organizations on which the Committee had been asked for advice. The report also indicated the way in which the Committee thought a number of other problems should be tackled in the future, including beriberi, nutritional anaemia, avitaminosis A, and other nutritional deficiencies affecting the eyes. One section of the report dealt with the organization and evaluation of nutritional studies and it was emphasized that education should figure prominently in the programmes.

Food additives

A review of the second report of the Joint FAO/WHO Expert Committee on Food Additives has already appeared in the Chronicle.[1] In the discussion of the report by the Board, emphasis was laid on the importance of the Joint Committee's first recommendation, namely, that FAO and WHO should give every possible encouragement to research studies that might further the development of better methods for evaluating the safety of food additives. Dr Habernoll (Federal Republic of Germany) supported the recommendation that the problem of the carcinogenic and mutagenic action of food additives should be studied by a special group of experts; and he endorsed the conclusion that no proved carcinogen should be considered suitable as a food additive in any amount. He also commented that foreign substances added unintentionally to food were at least as important as intentional additives. In reply, it was stated that such substances would form the subject of future investigations.

Reports of study groups

Requirements for biological substances

It was explained on behalf of the Director-General that it was the object of WHO to draw up recommendations on aspects of the control of biological substances outside the terms of reference of the Expert Committee on Biological Standardization. A study group had been convened to give advice on these questions. The group, which met from 7 to 12 October 1957, was of the opinion that

[1] *Chron. Wld Hlth Org.*, 1958, **12**, 52

national control authorities would be helped by having at their disposal detailed international recommendations on methods of assay and requirements for biological substances; and that the acceptance of such recommendations would greatly facilitate the exchange of biological substances between countries.

The group considered requirements in respect of a number of vaccines, toxoids and antitoxins, and drew up a general procedure for use in formulating international recommendations. First, an expert on the substance in question would be asked to prepare an initial draft, which would then be circulated to members of expert advisory panels and to national control laboratories for comment. Subsequently, the definitive recommendations would be drawn up by a group of experts and the final draft submitted to Member States. Final acceptance of the recommended requirements would, of course, be left to the discretion of the national authorities.

Chemotherapy and chemoprophylaxis in tuberculosis control

As a number of countries had sought the help of WHO in organizing tuberculosis control programmes based on domiciliary chemotherapy, the Director-General had decided to call together a group of experts to advise how such programmes could best be carried out. This group met from 23 to 25 September 1957, and its report has already been published.[2] The main conclusions of the group are:

(1) Tuberculosis prevalence surveys should be encouraged.

(2) All known cases of pulmonary tuberculosis should receive chemotherapy; in areas with a high prevalence of tuberculosis and inadequate facilities, this could be given on an ambulatory or domiciliary basis.

(3) Emphasis should be placed on the development of the most effective type of service for domiciliary chemotherapy.

In putting forward a minimum programme, the group emphasized that its recommendations are intended to serve as a guide for pilot projects in selected areas, rather than for country-wide control operations. It recommended provisionally that, in areas of high prevalence, isoniazid (INH) might also be administered prophylactically to tuberculin reactors living in the same household with infectious patients.

In the discussion of the report, several speakers underlined the importance of ensuring an adequate food supply for the patient and his family. Dr Moore (Canada) said that nutritional status was the crux of the whole problem. Under the Canadian tuberculosis programme among Indians, it was the practice to remove under-nourished patients from their families. The whole family was then given an adequate food supply over a six-month period, after which its members were re-examined. The supply of food was kept up after the patient had returned to his family until all danger of relapse was over. It was further pointed out by Dr Metcalfe (Australia) that the breadwinner of a family would resist attempts to make him give up his work and have treatment unless some provision were made for his family. The removal of sources of infection of tuberculosis was a fundamental consideration which, he thought, had not received sufficient emphasis in the report.

In the reply on behalf of the Director-General, it was agreed that an adequate standard of nutrition has long been recognized as a very important factor in resistance to tuberculosis and that the wisdom of providing chemotherapy in countries of low nutritional standards has often been questioned. On the other hand, a research project set up in Madras two years previously with the help of WHO has indicated that, even under these conditions, the patient given domiciliary treatment with drugs makes as much progress as the patient given hospital treatment over a lengthy period.

Classification of atherosclerotic lesions

In 1955, a Study Group on Atherosclerosis and Ischaemic Heart Disease drew attention to the urgent need for the standardization of

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 141

pathological criteria and terminology in respect of atherosclerosis, ischaemic heart disease and related conditions, and suggested that WHO should call a meeting of experts to study this question. A Study Group on Classification of Atherosclerotic Lesions was accordingly convened by the Director-General, with assistance from the United States Public Health Service. The report before the Board contained a terminology and definition of terms recommended by the Study Group for the description of conditions observed post mortem, and detailed methods for classifying and grading atherosclerotic lesions. The group had noted that there were marked geographical differences in mortality and morbidity from these conditions. Recommendations were also made regarding the co-ordination of environmental and epidemiological studies through regional centres, laboratories and hospitals. The suggestions were along similar lines to those followed by WHO in other fields, but the full implications have still to be worked out.

Histological definitions of cancer types

The decision to convene a study group on this question was the result of a resolution adopted by the Executive Board at its seventeenth session requesting the Director-General to "explore the possibility of WHO's organizing centres in several places in the world which would arrange for collection of human tissues and for their histopathological examination". A start has been made with types of cancer, and the Study Group, at its meeting from 24 to 28 June 1957, recommended that tumours of the oropharynx, lung, soft tissue and breast should be studied first. It was proposed that international centres should be set up for each of these types of tumour and the need for co-ordination with appropriate international non-governmental organizations was stressed. In reply to questions regarding the implementation of the group's recommendations, it was stated that an Expert Advisory Panel on Cancer had been established, and as a first step participants in the group had been appointed to it. Representation would be broadened later. It had been decided to give priority to lung tumours and soft tissue tumours, and negotiations were under way with two institutes that might serve as suitable international centres. It was agreed that it was important to avoid overlapping with work being done elsewhere and that the work must be conducted in co-operation with the International Union against Cancer.

Venereal disease in merchant seamen

Under the Protocol signed at the International Health Conference in New York in 1946, WHO took over the administration of the Brussels Agreement of 1924, respecting facilities to be given to merchant seamen for the treatment of venereal diseases. Following suggestions by the Health Assembly and the Executive Board that this agreement might be revised and broadened, the Director-General convened a study group in 1956 to consider what steps might be taken. Its report was circulated at the twentieth session of the Board, which had decided to consider the matter further at its twenty-first session. The main recommendations of the group were: that the Brussels Agreement should not be superseded by international health regulations and should not be abrogated unless similar provision were made in a broader agreement; that other nations should be asked to adhere to the agreement; that a technical committee of experts in the field of maritime public health and venereal-disease control should be convened periodically to advise WHO; and that the Director-General should consider arrangements for the provision of a scheme giving more comprehensive health services for seafarers in the major ports throughout the world. The Director-General had pointed out that before a decision could be taken on the last recommendation, an extensive study of the question would have to be made in co-operation with the International Labour Office, and this would take some time. The great value of the Brussels Agreement, which was the first international agreement of its kind, was stressed by speakers in the discussion, but it was the general opinion that joint studies

with ILO should be put in hand as soon as possible with a view to devising a scheme by which " health services could be provided in major ports to seafarers of all nationalities on a wider scale than at present". A resolution to this effect was subsequently adopted by the Executive Board.

Technical Conference on Insect Resistance

In July 1957, a technical conference was held in Geneva for the purpose of stimulating and co-ordinating an international research programme on the problem of resistance to insecticides. The conference was attended by directors of the major laboratories, who unanimously agreed to participate in an international programme of research and to extend an invitation to do so to laboratory directors not present at the conference. After a thorough study of the many aspects of the problem, they drew up a list of specific recommendations for organizing and carrying out the programme.

Dr Jafar (Pakistan) asked questions about the resistance of *Anopheles gambiae* and of flies to DDT. In reply it was stated that there was no record of resistance to DDT in *A. gambiae*. Some observations made by Dr Muirhead-Thompson in 1948 had been interpreted by reviewers as indicating a developed behaviouristic resistance. In fact they had shown that the spraying techniques had been at fault, so that the insects received an exciting dose instead of a lethal one and escaped from the sprayed surfaces into window traps.

With regard to flies, it was explained that the development of resistance was essentially a process of Darwinian selection. In the original population, the genes responsible for resistance were extremely rare, whereas in the population surviving insecticide treatment a high proportion of the insects carried these genes. When spraying with DDT-like insecticides was first used against flies, the fly population was reduced almost to the point of disappearance. Later it was discovered, however, that there were a very few survivors resistant to the insecticide, and that when spraying was continued the percentage of survivors increased with each generation. Resistance to dieldrin appears to be acquired more readily than resistance to DDT and there is also the possibility that the use of dieldrin increases the number of eggs laid by survivors. Dr Togba (Liberia) stressed the importance of this phenomenon in connexion with the use of dieldrin in malaria eradication programmes and stated that he had seen places that were teeming with flies as a result of spraying with dieldrin.

* * *

The Executive Board authorized the publication in the Technical Report Series of the World Health Organization of all the reports of the expert committees, with the exception of the one concerned with the International Pharmacopoeia (see page 85). Responsibility for authorizing publication of the reports of study groups and conferences rests with the Director-General.

Epidemiological and Statistical Information

YELLOW FEVER IN 1957

According to a note published in a recent issue of the WHO *Weekly Epidemiological Record* (No. 5, 1958), 74 cases of jungle yellow fever were officially notified in America during 1957, including 35 in Colombia, 19 in Bolivia, 10 in Brazil, 5 in Venezuela, 3 in Peru and 2 in Panama. In Africa, 3 cases were reported in 3 local areas of the Belgian Congo, and 2 suspected (unconfirmed) cases in Nigeria.

Two of the accompanying maps show the distribution of these cases, while the third indicates the northward movement of yellow fever in Central America during 1957, as revealed by the presence of the disease in vertebrates other than man in Sayaxché Municipio, Peten Department, Guatemala, and in the Cayo district of British Honduras.

YELLOW FEVER IN 1957

A = *Human cases notified in 1957*
B = *Presence of yellow fever in vertebrates other than man*
S = *Suspected cases*

Notes and News

Re-introduction of malaria

The need for measures to prevent the re-introduction of malaria into areas where the disease has been eradicated—or where its eradication is under way—is recognized by the WHO Committee on International Quarantine in its fifth report [1] which was discussed by the WHO Executive Board at the latter's twenty-first session. In considering this topic, the Committee had before it the report of the WHO Study Group on International Protection against Malaria,[2] which met in Amsterdam in December 1956, and the sixth report of the WHO Expert Committee on Malaria.[3]

The disease may be re-introduced either by infected persons or by insect vectors. Of the latter, those which have developed resistance to insecticides present a special danger.

The risk of the re-introduction of malaria by infected persons is greatest during or after the final, or "maintenance", stage of an eradication campaign, when positive measures to prevent the transmission of the disease are no longer being taken and the active surveillance mechanism for the detection of cases has been replaced by the normal vigilance of the public health service. At this stage, a careful watch should be kept for primary cases among new arrivals in the area, and for secondary cases in their vicinity.

These new arrivals may be divided into the following categories: international travellers, including tourists; migrants, including seasonal workers or permanent settlers; and such groups as nomads or pilgrims.

International travellers normally arrive singly, or in small groups (couples or families), and their stay is usually short. Secondary cases arising from the re-introduction of malaria by persons in this category are likely to be few in number and relatively circumscribed as regards time and place of occurrence. When the disease is re-introduced by persons in the other categories—who will generally arrive in greater numbers and, in most cases, will stay for some time—secondary cases will probably be much more numerous and scattered, spaced out over a longer period, and less easy to control.

The Committee was of the opinion that there is no need for international travellers to be subjected to special antimalaria measures before entering areas of eradication. On the other hand, it might be desirable for antimalaria drugs to be administered to all migrants and participants in "periodic mass congregations" proceeding to such areas. Measures to this effect have already been found necessary in French Guiana. Amendments to the International Sanitary Regulations in this connexion are not, however, contemplated for the moment, nor is there as yet any question of declaring malaria a quarantinable disease.

The development of resistance to insecticides among insect vectors of malaria has been known to cause the temporary failure of control or eradication programmes. The transference of resistant vectors to areas where eradication programmes using the same insecticides are in progress would almost certainly have the same result.

The Committee considered that the strongest defence against the importation of mosquitos by sea or air is the rigid protection of ports of entry by antimosquito measures, and endorsed a recommendation by the Study Group on International Protection against Malaria that health administrations concerned "should be asked to take all reasonable possible steps to this end". Disinsectization of aircraft on or before arrival may also be necessary, and— in cases where there

[1] Unpublished working document WHO/IQ/61
[2] Unpublished working document WHO/Mal/183
[3] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 123

is reason to expect the importation of insect vectors of disease—this measure could be applied to other modes of transport as well.

Resistance to DDT in *Anopheles stephensi*

Anopheles stephensi is an important vector of malaria in several of the Eastern Mediterranean countries and in South-East Asia. After spraying with DDT had been carried out successfully against this mosquito for periods up to 10 years, resistant strains recently began to emerge. Resistance was first confirmed late in 1955 in the Dhahran area of Saudi Arabia, where DDT had been in use since 1947. Suspicion had been aroused the previous year by an increase in the number of house-resting *A. stephensi* and by a rise in parasite and spleen rates. Susceptibility tests carried out by Mr G. Davidson, WHO consultant, confirmed that resistance had developed in areas sprayed with DDT but not in an unsprayed area. Susceptibility to dieldrin and to BHC was normal in both treated and untreated areas.

During 1957, strains of *A. stephensi* resistant to DDT made their appearance in Iran and Iraq. In Iran, DDT spraying had been in progress for 5-6 years. The first indication that resistance had developed was an epidemic of malaria affecting between 8000 and 15 000 people in the Abadan area, a part of the country that had been practically free from malaria for the previous three years. Another outbreak occurred in the Shadegan area. Susceptibility tests showed that resistance to DDT in *A. stephensi* extended to nearly all the area of distribution of this species in Iran. The population affected is approximately 1 300 000. The Iranian Government, in consultation with WHO, has decided to replace DDT by dieldrin in the next spraying operations throughout the entire area of distribution of *A. stephensi*.

A study carried out by a WHO Advisory Team on Malaria Eradication in southern Iraq showed that DDT resistance in *A. stephensi* had also developed in Basra (near the Abadan area of Iran) and in the neighbourhood of Nassriya. In Basra, DDT larvicide had been in use since about 1947 and DDT imagocide since 1954, but in the Nassriya area DDT spraying had been carried out for the first time in April 1957 against adults only. The fact that resistance was found in both adults and larvae in this area is therefore a rather alarming development. As in Iran, susceptibility to dieldrin and BHC was normal, and the Iraq Government has decided to replace DDT by dieldrin in all malarious areas where *A. stephensi* is the vector. There is a population of about one million living in the affected areas.

Preliminary accounts of the observations on DDT resistance in *A. stephensi* made in Iran and Iraq were presented at the last WHO Regional Technical Meeting on Malaria Eradication, held in Baghdad from 7 to 12 December 1957, and will shortly be published in the WHO Bulletin.

Dieldrin resistance in *Culex pipiens fatigans* in Malaya

Resistance to insecticides in *Culex pipiens fatigans* has already been reported from two areas in Malaya. In Penang two years' use of BHC as a larvicide resulted in the development of a strain which was found to have acquired a tenfold resistance to BHC, and also to dieldrin to which it had not been exposed. In Singapore, when larval control became unsatisfactory after 6 months' use of a dieldrin emulsion, laboratory experiments confirmed that active resistance to dieldrin had developed. The latest observations, as reported by R. H. Wharton in an article on the resistance of *Culex pipiens fatigans*, which will shortly appear in the WHO Bulletin, deal with the finding of two further dieldrin-BHC resistant strains of *C. p. fatigans* in Malaya, but differ from the previous reports in that resistance, in one strain at least, was developed as a result of house-spraying with dieldrin against adult mosquitos. In this strain, resistance to dieldrin was about 100 times greater than normal in both adults and larvae, and resistance to gamma-BHC in larvae about 20 times greater, while resistance to DDT was slight.

Improvements in the casting of water-seal latrines

The hand-flushed, water-seal latrine is not only fly-proof, but—if the bowl and slab are kept clean—odourless. A further advantage is that its design makes it impossible for children and small animals to fall into the latrine pit. An inexpensive method of casting water-seal latrine bowls in cement mortar and incorporating them in concrete slabs was first developed on a WHO project in Chiengmai, Thailand, and has been described in the WHO Bulletin.[1]

Two interesting modifications in this method have been introduced at Trivandrum, India, further reducing costs and permitting a greater use of locally available material.

The first modification is in the moulding of the bowl and trap. Originally a separate clay form was used for the interior of the trap. This has now been replaced by a wooden form, which is attached by a dowel to the main (wooden or concrete) body of the mould during mortaring, but can be lifted off with the bowl when the cement has hardened. The shape of the form permits its withdrawal from the finished trap. The whole process of tempering and moulding clay, and subsequently digging it out of the trap, has thus been eliminated.

The second modification consists of reinforcing the concrete slab with bamboo strips, 2-3 cm wide, in place of light wire mesh (chicken wire). Preliminary tests suggest that this method of reinforcement—which has reduced latrine construction costs at Trivandrum by about 16%—imparts greater strength to the slab.

Preservatives in milk

For many years, one of the chief problems in the milk industry—especially in warm climates—has been that of keeping milk fresh, particularly while it is awaiting delivery to a pasteurizing or processing plant. The use of rapid transport and refrigeration for this purpose may be costly and cannot provide a practicable solution in every case.

A group of experts, convened by the Food and Agriculture Organization of the United Nations (FAO), therefore met at Interlaken, Switzerland, from 23 to 27 September 1957, to discuss the possibility of using preservatives, notably hydrogen peroxide, to overcome the problem. WHO was represented at this meeting by Professor H. D. Kay, Director of the National Institute for Research in Dairying, United Kingdom, and Dr. I. Nir-Grosfeld, of the Health Laboratory Methods Section, WHO Headquarters.

According to the general principles formulated by the Joint FAO/WHO Committee on Food Additives,[1] decisions on the use of any form of food additive should be based, above all, on evidence of its safety.

In the case of hydrogen peroxide, this evidence is not at present sufficient to warrant its use as a preservative in milk. The meeting was generally of the opinion that the use of this or any other preservative in milk is undesirable, and should be considered only in exceptional circumstances.

Expert Committee on Medical Rehabilitation

The problem of physical disability has received much attention in recent years, both from government authorities and voluntary organizations. Today, a great deal can be done to restore physically handicapped persons to a comparatively normal life, thanks to new concepts and methods of rehabilitation (medical, social, educational and vocational).

The WHO Expert Committee on Medical Rehabilitation met in Geneva during February to review the basic principles and aims of medical rehabilitation and discuss the planning and organization of medical rehabilitation services, with particular reference to the less developed countries.

The following experts took part in the meeting: Dr F. S. Cooksey (United Kingdom), Dr G. Harlem (Norway), Dr H. H. Kessler (USA), Dr M. Maurer (Romania), Dr E. Mindus (Sweden), Dr F. E. Godoy Moreira (Brazil), Professor J. Parisot (France), and

[1] *Bull. Wld Hlth Org.*, 1956, **14**, 816

[1] See *Wld Hlth Org. techn. Rep. Ser.*, 1957, **129**.

Dr R. Soeharso (Indonesia). Representatives from the United Nations and ILO also took part in the meeting.

Sanitation of international airports

In 1951, the Fourth World Health Assembly, reviewing general public health problems arising from air travel, stressed the need for protecting the health of aircrews on international flights. It advocated the control at international airports, not only of the quarantinable diseases covered by the International Sanitary Regulations, but also of such diseases as dysentery, food-poisoning, gastro-enteritis and malaria. The Assembly recommended that WHO set up a Committee, in collaboration with the International Civil Aviation Organization (ICAO), to prepare a guide for use by health administrations in the sanitary control of international airports.

As a first step in this direction, WHO drafted a document on the hygiene and sanitation of air travel. This document was discussed with ICAO and circulated for comment to experts in a number of countries. A new draft, prepared on the basis of the comments received, was one of the main subjects of discussion at a meeting of the WHO Expert Committee on Sanitation of International Airports, held in Geneva during March.

The purpose of the meeting was to review the special sanitation problems associated with air travel, to study the relationship of airport sanitation to the general public health programmes of airports, and to recommend appropriate administrative and technical measures.

The following experts took part: Mr S. Haegerström (Sweden), Professor A. El Halawani (Egypt), Mr Malcolm C. Hope (USA), M. R. Maurel (France), Dr Edgar Tostes (Brazil), and Sir Harold Whittingham (United Kingdom). The meeting was attended by two observers from ICAO.

Dental health services for children

Regular dental examinations, early treatment of caries, and preventive measures —brushing, suitable diet, and the use of fluorides—are necessary for the protection of the teeth. Such protection must obviously begin in childhood, and it is therefore important that there should be good dental services in schools and for children generally.

As neglect of the teeth is a widespread cause of ill-health in Europe, a Study Group on Dental Health Services for Children, sponsored by the Belgian Government and the WHO Regional Office for Europe, was convened at Brussels in February. The purpose of the meeting was to study existing dental health services for children in Europe, and to make suggestions for their improvement and the development of new services.

The Study Group included participants from Belgium, Bulgaria, Denmark, Finland, France, Germany, Ireland, Italy, Netherlands, Norway, Sweden, Switzerland, the United Kingdom, USSR and Yugoslavia.

Seminar on the resistance of insects to insecticides

Increasing insecticide resistance is becoming a serious threat to the success of vector control and eradication programmes. A seminar on this urgent problem was therefore convened by WHO, from 26 February to 7 March, at New Delhi, on the invitation of the Government of India. Its aim was to encourage and develop research on insecticide resistance by enabling biologists and entomologists working in this field to pool their knowledge and techniques, and evolve some form of corporate attack on the problem.

The seminar had 54 participants from the following countries and territories in the Western Pacific, South-East Asia and Eastern Mediterranean Regions: Australia, Egypt, Hong Kong, India, Iran, Israel, Japan, Lebanon, Malaya, New Zealand, Pakistan, Philippines, Saudi Arabia and Taiwan (China).

Nutrition publications

The Food and Agriculture Organization of the United Nations (FAO) has recently issued two publications of interest to public

health workers and nutritionists, which are the outcome of work done in collaboration with WHO.

The first of these publications, *Principles of Milk Legislation and Control* by W. A. Lethem (Agricultural Development Paper No. 59), is the result of the common interest of FAO, UNICEF and WHO in the field of milk hygiene. It has been produced through the efforts of the Inter-Agency (FAO/UNICEF/WHO) Working Group on Milk Products which was set up to study problems of increasing milk production and consumption, keeping in mind the necessity of ensuring that the product is nutritious, wholesome and not a danger to public health. This publication aims at outlining the legislation and control which may have to be introduced in order to ensure that milk and milk products, as they reach the consumer, are clean, wholesome and safe.

Contents: Administration. Special provisions for hot climates. General requirements. Special requirements during conveyance and distribution. Special types of milk. Milk products. Tests. Conclusions.

The author, a barrister-at-law and consultant to FAO, was lately Principal Medical Officer, Ministries of Health and Food, United Kingdom. The price of this 68-page brochure is 3/9, or US $0.75. French and Spanish editions are also available.

The second publication, *Report of an International Seminar on Education in Health and Nutrition* by F. W. Clements (Nutrition Meetings Report No. 13), deals with a seminar held by FAO and WHO at Baguio, Philippines, in 1955 with 58 participants from 22 nations. In the words of the author, this report " attempts to record progressively the thinking and the reactions of a group of people brought together for a period of time to discuss common problems in the field of health and nutrition education ". Divided into three parts, the report briefly tells the story of the seminar itself in Part I. Part II deals with detailed reports of the topics discussed, and Part III consists of appendices.

Contents: Main points emerging from the seminar. What the seminar meant to participants. How the staff saw the seminar. Learning about themselves and their problems. Learning about people. Learning and teaching. How to develop health and nutrition education programmes. Evaluation. Follow-up.

The price of this 92-page booklet, which is published in French as well as English, is 5/- or US $1.00.

People and Places

Leprologist visits Iran and Ethiopia

A well-known French leprologist, Dr Paul Laviron, recently went to Iran, on behalf of WHO, to assist the Iranian Government in launching a new leprosy control project. Dr Laviron will also visit the WHO/UNICEF-assisted leprosy control project in Ethiopia.

Dr Laviron has worked as a leprologist in the French territories of Oceania and West and Equatorial Africa for more than twenty years, and is a member of the WHO Expert Advisory Panel on Leprosy. His work in developing the injectable suspension of DDS (diamino-diphenyl-sulfone) in chaulmoogric media has greatly facilitated the mass treatment of the disease.

Nutrition study in Northern Rhodesia

In connexion with a general scheme for rural development, the Government of Northern Rhodesia is conducting research into the relationship between diet and parasitic diseases, and their effect on health. To assist in this task, WHO has sent a medical nutritionist—Dr Bent Friis-Hansen, of Denmark—to Northern Rhodesia for a period of one year. Another WHO consultant, Dr Fergus S. McCullough, has already carried out a survey of parasitic diseases in the area.

A graduate of the University of Copenhagen, Dr Friis-Hansen has studied metabolism at the Harvard Medical School, and is also a specialist in paediatrics.

WHO team for tuberculosis project in Kenya

A five-member team has been formed by WHO to assist the Government of Kenya in research on the use of chemotherapy and chemoprophylaxis in tuberculosis control. The team, which is expected to arrive in Kenya in April, will first carry out a survey of the prevalence of tuberculosis in Nairobi, where a

random sample of the population will be examined. Cases will be treated at home, and an attempt will be made to find the most efficient way of administering chemotherapy on a large scale in an African population.

The leader of the team is Dr Tage Egemose, of Denmark, who has studied anti-tuberculosis work in the United States and has taken part in internationally assisted BCG campaigns in Europe and South America. Dr E. Mossige, of Norway, the bacteriologist on the team, participated in a number of WHO-assisted projects in the South-East Asia and Eastern Mediterranean Regions during the past seven years. The statistician, Mr Jon Thillemann, of Denmark, has been with WHO for several years, working for most of the time at the Tuberculosis Research Office in Copenhagen. Miss Fay Ashton, the team's public health nurse, is British, and has worked for more than four years on a WHO-assisted tuberculosis project in Pakistan. The laboratory technician, Mr Alfred Beer, who is also British, has worked in various laboratories in the United Kingdom.

Organization of mental health service in Iran

WHO has appointed Dr Geoffrey Tooth as Mental Health Adviser to the Government of Iran for a period of two months, starting in February. His duties will include: advising the Government on the organization of a mental health service—both preventive and curative—within the framework of the public health services; advising the Ministry of Education on juvenile delinquency problems and the development of child guidance clinics; and helping to organize psychiatric training for medical personnel and mental health workers in general.

Dr Tooth is a Commissioner of the Board of Control, Ministry of Health, London, where his work involves the inspection of psychiatric and mental deficiency institutions. He has carried out research on mental health problems in Ghana and Nigeria, and in 1956 acted as consultant to the WHO Expert Committee on Mental Health.

Health education adviser for India

A WHO health education adviser—Dr Hartmut Dix—went to Nagpur, India, in February to assist in planning and developing health education services in Central Province. Dr Dix, who has a degree in public health from the University of California, was Director of Health Education in the Ministry of Health for Germany.

Re-drafting of public health legislation

The Government of Ceylon plans to bring its public health legislation more into line with modern requirements. Dr Frederick Grundy, Professor of Preventive Medicine in the Welsh National School of Medicine, Cardiff, has gone to Ceylon, on behalf of WHO, to advise the Government in this connexion. Professor Grundy, who is a barrister-at-law, held many executive posts in public health before taking up an academic career. His published work includes the WHO monograph *Teaching of Hygiene and Public Health in Europe*, which he wrote in collaboration with Professor James Mackintosh.

Professor Grundy will he joined later by Mr E. H. Watson, Senior Legal Assistant of the Ministry of Health, London. Mr Watson has twenty-five years' experience of the legal and administrative aspects of public health legislation. He will be responsible for the preparation of such new and amended legislation as may be found necessary, for presentation to the legislature of Ceylon.

Training of malariologists

Dr Alan Gilroy went to Iraq in February, on behalf of WHO, to give a training course to future malariologists. Educated at the University of Melbourne and the London School of Hygiene and Tropical Medicine, Dr Gilroy has been associated for some twenty years with malaria and its control in various countries, including New Guinea, Nigeria, Ghana and India.

Pool of advisers on malaria eradication

A pool of advisers has been created in the Division of Malaria Eradication, WHO Headquarters, to assist countries in planning eradication campaigns and provide them with technical advice when the campaigns are in progress. The members of this pool are Dr Perez Yekutiel, Dr Jean Lavergne and Dr G. Houel.

After a month's general briefing at WHO Headquarters, the three malariologists will spend some two months in Latin America, visiting eradication campaigns in Mexico, Venezuela and other countries. They will then return to Geneva, where they will be available for assignment—as leaders of pre-eradication survey teams or of advisory groups—to countries requesting advice.

Dr Yekutiel has been Director of the Division of Epidemiology in the Ministry of Health, Israel, for the last six years. He has carried out malaria surveys and control work in several countries of the Eastern Mediterranean Region.

Dr Lavergne is a former Medical Adviser to the French Army, and has worked on parasitology in Cameroun and Viet Nam. From 1947 to 1949, he was Director of the Malaria Services in Madagascar, where he carried out several field operations and was

responsible for chemoprophylaxis among the French troops. He has more recently held public health appointments in French West Africa and Laos.

Dr Houel has worked in Morocco as Chief of the Malaria Service in charge of general prophylaxis and epidemiology, and also as Chief of the Preventive Section of the Ministry of Health. In the latter capacity, he directed BCG, antitrachoma and anti-syphilis campaigns in collaboration with WHO and UNICEF.

Other staff changes at WHO Headquarters

Dr Constantin Vinokouroff, of Moscow, has been appointed Director of the Division of Therapeutic Substances at WHO Headquarters, Geneva. He succeeds Dr W. A. Timmerman, who was recently appointed Assistant Director-General in charge of the Department of Central Technical Services.

Educated at the University of Moscow, Dr Vinokouroff was associated with the development of WHO in the early days of the Organization, serving as the adviser of the USSR delegation to the fifth session of the WHO Interim Commission and the First World Health Assembly. As representative of the USSR Academy of Medical Sciences, he has taken part in international scientific conferences in Iran, Germany, Italy, Denmark, Switzerland, Poland, France and Albania. Prior to his appointment with WHO, Dr Vinokouroff was Department Chief at the Neurological Institute of the USSR Academy of Medical Sciences.

* * *

Dr R. Lowry Dobson, from the University of California, Berkeley, California, USA, has been appointed to Headquarters to assist in WHO's programme concerning the peaceful uses of atomic energy in relation to health. A graduate of the University of California, Dr Dobson received his A.B., his M.D. and later his Ph.D. in Biophysics from this University. Since 1947 he has been Medical Director of the Health Protection Group in the University of California Radiation Laboratory and has had considerable teaching and research experience in the University. He has also been engaged in work connected with the clinical use of radioisotopes. Most of Dr Dobson's published work is concerned with various aspects of the biological effects of radiation.

* * *

Dr Edward Grzegorzewski has been granted special leave of absence from his post as Director, Division of Education and Training Services, WHO Headquarters, so that he may take up appointments in the USA and Puerto Rico. The first of these appointments is as visiting Professor of Public Health for the year 1957/58 at Johns Hopkins University, Baltimore, Md., and the second as Professor of Preventive Medicine and Public Health, and Director of the corresponding Department, at the University of Puerto Rico, San Juan.

Review of WHO Publications

BILHARZIASIS

Intermediate hosts of Schistosoma: African Biomphalaria and Bulinus, by G. Mandahl-Barth, Geneva, 1958 (*World Health Organization: Monograph Series*, No. 37), 132 pages. Price: £1, $4.00, or Sw. fr. 12.—. French edition in preparation.

The nomenclature of the snails which serve as intermediate hosts for bilharziasis, particularly those species belonging to the genera *Biomphalaria* and *Bulinus* in Africa, has been in a state of confusion for many years. A number of factors have been responsible for this. The original description of a species, for example, was often so brief and generalized that it is not now possible to be certain what species was being described. Frequently the exact locality where the type material was found is not known, thus preventing the collection of topotype material from which a fuller description of the species, particularly the anatomy, could be made. Since it was a common practice among certain authors to name indiscriminately the extremes found within the normal range of variation in a single species, the majority of the now-recognized species of

snails are known under a variety of names. Unfortunately, moreover, there have been too few malacologists competent to determine correctly the species belonging to these two genera.

During the past few years WHO has attempted to improve this situation. On two occasions, specialists in malacology from several countries have been assembled to discuss the taxonomic problems in the hope that agreement could be reached which would unify the nomenclature used in the determination of this group of snails. Snail Identification Centres have been established at Copenhagen, Paris and Salisbury to which collections could be forwarded for identification and where students might study and compare well-preserved material from various parts of Africa and come to a better understanding of the range of variation to be found among these snails.

This monograph—the first comprehensive study from one of these Centres—is based on the examination of a large number of specimens from many localities, which have been compared with the original descriptions and, whenever possible, with type material. The conclusions it presents have been critically reviewed by several malacologists who also have had considerable experience with these two genera. They encountered some difficulty in attempting to appraise this work accurately, however, because of the disparity of the material which each one had studied: these was also disagreement with some of its conclusions, owing to differences of opinion on the concepts of species, sub-species and ecophenotype. Only additional research on specimens collected from the localities which provided the material studied in this work, and the collection and examination of further material from areas where little or nothing is known regarding the species, subspecies, and variations, will make it possible to establish a recognized and stable nomenclature. There was unanimous agreement among the scientists, however, that Dr Mandahl-Barth's comprehensive study would serve as an invaluable basis for more advanced research and a better understanding of the species of these African snails.

ENDEMIC GOITRE

Bulletin of the World Health Organization, 1958, Volume 18, Number 1-2 (pages 1-274)

" Goitre . . . occurs with varying intensity in almost every country; few countries appear to be entirely free from it. The disease has been observed in the far north, in the tropics, and in the far south; it occurs quite independently of climate, season or weather. Moreover, in its incidence goitre makes no distinction of race, nationality, colour, creed or class; the North American, the European, the Chinese, the Himalayan Indian, the Turkoman, and the peoples of Central and South America all suffer from it under certain conditions—some severely, some moderately, some but mildly."

The above are the opening words of the first article in this issue of the *Bulletin of the World Health Organization* [1]—a world survey by F. C. Kelly & W. W. Snedden of the prevalence and geographical distribution of endemic goitre—and they emphasize the global nature of the goitre problem today. Endemic goitre is not a " killer " like malaria or cholera, but it nevertheless has serious repercussions on the physical, social and economic well-being of any population in which it is rife. Through its direct effects on afflicted persons—discomfort, disfigurement and apathy—and its indirect consequences—increased incidence of certain grave pathological conditions—it is responsible for much human misery and suffering.

In 1952, recognizing the public health significance of the disease, the World Health Organization convened a group of experts to study the matter. The report of this study group, as well as a number of individual papers dealing with various aspects of the control of endemic goitre, was subsequently published in the Bulletin (Vol. 9, No. 2), in the hope that the information would be of assistance to governments interested in investigating the goitre position in their own territories. In the four years that have

[1] For the list of contents, see the advertising section at the end of this issue of the Chronicle.

elapsed since this publication appeared, a considerable amount of further information on the goitre problem has come to light, and it was felt that it would be useful to publish a second collection of papers. It is hoped that this second collection, which is now published in the Bulletin, will eventually be revised and re-issued, together with some additional material to make the treatment of the subject as comprehensive as possible, in monograph form. Since the monograph will be published in separate English and French editions, the summaries in the other language that are usually included at the end of articles in the Bulletin have not been provided in this issue.

After Kelly & Snedden's world survey of endemic goitre follows a contribution by F. W. Clements, who discusses the natural history of the disease in affected persons and reviews the present state of knowledge regarding the occurrence of cretinism, deaf-mutism and mental deficiency in the offspring of goitrous parents—a subject that is still, to a large extent, a matter for controversy.

" Insight into the nature of thyroid disease " writes J. B. Stanbury in the next article, the third in this series of papers, " has developed through an understanding of the normal function of the thyroid gland. " In his article, Stanbury gives a brief outline of what is currently known of the physiology of the thyroid and of the metabolic circuit of iodine and summarizes the information available regarding the functional abnormalities of the human thyroid when it is deprived of iodine.

The results of goitre surveys carried out in various parts of the world will not be strictly comparable unless uniform techniques are employed. C. Pérez, N. S. Scrimshaw & J. A. Muñoz, discussing the classification of goitre and the technique of goitre surveys in the fourth article, stress the importance of adopting methods that " will result in data which can be used with confidence to guide public health programmes ". This interesting contribution outlines procedures for selection of population samples, examination, classification of goitres, and tabulation and presentation of survey data, etc. that have " proved practical and useful under a wide variety of conditions ".

The next article deals with the important question of the treatment and prevention of endemic goitre. J. Matovinović & V. Ramalingaswami trace the history of goitre therapy and prophylaxis from their earliest days up to the present, pointing out the mistakes that were made in the past and the developments that have taken place in recent years. They draw attention to some recent work by Clements that may prove to be of importance in some areas. There is, it appears, in Tasmania a naturally occurring goitrogenic substance which seems to have the capacity to inhibit the iodine-trapping mechanism of the thyroid, and in these circumstances treatment with iodine may be of no avail. It is quite clear, however, that where goitre is demonstrated to be due to an iodine deficiency its control should be a simple matter, and the authors conclude their paper with the much-quoted opinion of David Marine, a pioneer of modern goitre prophylaxis: " Simple goitre is the easiest of all known diseases to prevent . . . It may be excluded from the list of human diseases as soon as society determines to make the effort."

The control of endemic goitre is usually merely a matter of making good the iodine deficiency of the affected population. In practice, however, the provision of supplementary iodine presents certain technical problems. Salt, the most widely used vehicle for the iodine, varies in quality from the fine, free-running product available in highly developed countries to the coarse substance common in less developed areas, and different techniques for iodization are therefore required. In the last paper in this series, J. C. M. Holman describes various iodization processes, including some simple and inexpensive ones specially designed for use in regions where the people are accustomed to using local supplies of crude salt, and deals with other technical matters, such as the stability of iodized salt, the most suitable levels of iodization and the determination of iodine in common and iodized salt.

International Non-Proprietary Names for Pharmaceutical Preparations

In accordance with paragraph 3 of the Procedure for the Selection of Recommended International Non-Proprietary Names for Pharmaceutical Preparations (see Annex 1, page 109), notice is hereby given that the following names are under consideration by the World Health Organization as Proposed International Non-Proprietary Names.

Comments on, or formal objections to, Proposed Names may be forwarded by any person to the Pharmaceutical Section of the World Health Organization within four months from 1 April 1958.

The inclusion of a name in this list does not imply any recommendation for the use of the substance in medicine or pharmacy.

PROPOSED INTERNATIONAL NON-PROPRIETARY NAMES (*Prop. I.N.N.*): LIST 6 [1]

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
acenocoumarolum acenocoumarol	3-[α-(4-nitrophenyl)-β-acetylethyl]-4-hydroxycoumarin
acepromazinum acepromazine	2-acetyl-10-(3-dimethylaminopropyl) phenothiazine
acetazolamidum acetazolamide	2-acetamido-1,3,4-thiadiazole-5-sulfonamide
acidum edeticum edetic acid	ethylenediamino-*N,N,N',N'*-tetra-acetic acid
aldosteronum aldosterone	18-oxo-corticosterone
ambenonii chloridum ambenonium chloride	*N,N'*-bis-(2-diethylaminoethyl)-oxamide bis-2-chlorobenzyl chloride
ambucainum ambucaine	β-diethylaminoethyl 4-amino-2-butoxybenzoate
ambucetamidum ambucetamide	2-(di-*n*-butylamino)-2-(*p*-methoxyphenyl)-acetamide
aminometradinum aminometradine	1-allyl-3-ethyl-6-amino-2, 4-dioxo-1,2,3,4-tetrahydropyrimidine
amiphenazolum amiphenazole	2,5-diamino-4-phenylthiazole

[1] Other lists of proposed international non-proprietary names can be found in *Chron. Wld Hlth Org.*, 1953, 7, 297; 1954, 8, 216 and 313; 1956, 10, 28; 1957, 11, 231.

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
amisometradinum amisometradine	6-amino-1,2,3,4-tetrahydro-3-methyl-1-methylallylpyrimidine-2,4-dione
amolanonum amolanone	3-(β-diethylaminoethyl)-3-phenyl-benzofuran-2-one
azacyclonolum azacyclonol	α,α-diphenyl-α-piperid-4-yl-methanol
bemegridum bemegride	4-ethyl-4-methyl-2,6-dioxo-piperidine
benactyzinum benactyzine	2-diethylaminoethylbenzilate
benzonatatum benzonatate	2-(ω-methoxyoctaethyleneoxy)-ethyl *p*-butylaminobenzoate
betazolum betazole	3-(β-aminoethyl)-pyrazole
bietamiverinum bietamiverine	2-diethylaminoethyl α-phenyl-α-piperidinoacetate
busulfanum busulfan	1,4-dimethanesulfonoxybutane
calcii glucoheptonas calcium glucoheptonate	calcium hexahydroxyheptonate
captodiamum captodiame	*p*-butylthiodiphenylmethyl-2-dimethylaminoethyl sulfide
carbazochromi salicylas carbazochrome salicylate	adrenochrome monosemicarbazone sodium salicylate complex
chlorambucilum chlorambucil	*p*-di-(2-chloroethyl)-aminophenylbutyric acid
chlordimorinum chlordimorine	4-[γ-(4-morpholino) propoxy]-3-chlorobiphenyl
chlorhexidinum chlorhexidine	1,6-bis-(*p*-chlorophenyldiguanido)-hexane
chlorisondamini chloridum chlorisondamine chloride	4,5,6,7-tetrachloro-2-(trimethylammonium-ethyl)-*N*-methyl-*iso*indoline dichloride
chloroprocainum chloroprocaine	β-diethylaminoethyl 2-chloro-4-aminobenzoate
chlorotrianisenum chlorotrianisene	tri-(*p*-methoxyphenyl)-chloroethylene
chloroxylenolum chloroxylenol	4-chloro-3,5-dimethylphenol
cinnofuradionum cinnofuradione	4-tetrahydrofurfuryl-1,2-(benzo(c)-cinnolino)-pyrazolidine-3,5-dione
clidinii bromidum clidinium bromide	1-methyl-3-benziloyloxyquinuclidinium bromide
corticotrophinum-zinci hydroxydum corticotrophin-zinc hydroxide	a preparation of purified corticotrophin adsorbed on zinc hydroxide
crotamitonum crotamiton	*N*-ethyl-*N*-*o*-toluyl crotonamide

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
cryofluoranum cryofluorane	1,2-dichloro-1,1,2,2-tetrafluoroethane
cyclomethycainum cyclomethycaine	3-(2-methylpiperidino)-propyl *p-cyclo*hexyloxybenzoate
cycloserinum cycloserine	4-amino-isoxazolidin-3-one
demecolcinum demecolcine	deacetylmethylcolchicine
deserpidinum deserpidine	11-desmethoxyreserpine
dextromoramidum dextromoramide	*d*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine
dichlorophenum dichlorophen	di-(5-chloro-2-hydroxyphenyl) methane
dicycloverinum dicycloverine	β-diethylaminoethyl *cyclo*hexyl-*cyclo*-hexane-carboxylate
dimethoxanatum dimethoxanate	β-dimethylaminoethoxyethyl phenothiazine-10-carboxylate
dioxethedrinum dioxethedrin	1-(3,4-dihydroxyphenyl)-2-ethylamino-propan-1-o1
diphenadionum diphenadione	2-diphenylacetyl-1,3-indandione
diphenylpyralinum diphenylpyraline	*N*-methylpiperidyl-4-benzhydryl ether
dipyrocetylum dipyrocetyl	2,3-diacetoxybenzoic acid
dycloninum dyclonine	*p*-butoxy-3-piperidinopropiophenone
ecothiopati iodidum ecothiopate iodide	*o,o*-diethyl *s*-(2-trimethylammonium ethyl) phosphorothiolate iodide
endomycinum endomycin	an antibiotic substance obtained from cultures of *Streptomyces endus*, or the same substance produced by any other means
etamiphyllinum etamiphyllin	7-(2-diethylaminoethyl)-theophyllin
ethinamatum ethinamate	1-ethynyl*cyclo*hexyl carbamate
ethotoinum ethotoin	3-ethyl-5-phenylhydantoin
ethylphenacemidum ethylphenacemide	phenylethylacetylurea
ethypiconum ethypicone	4,6-dioxo-3-methyl-5,5-diethyl-1,4,5,6-tetrahydropyridine
etoxeridinum etoxeridine	1-[2-(2-hydroxyethoxy)-ethyl]-4-phenylpiperidine-4-carboxylic acid ethyl ester
florantyronum florantyrone	γ-fluoranthen-8-yl-γ-oxobutyric acid

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
fludrocortisoni acetas fludrocortisone acetate	9-α-fluoro-17-hydroxycorticosterone 21-acetate
fluoxymesteronum fluoxymesterone	9-α-fluoro-11-β-17-β-dihydroxy-17-α-methylandrost-4-ene-3-one
forminitrazolum forminitrazole	2-formamido-5-nitrothiazole
glucurolactonum glucurolactone	γ-lactone of D-glucofuranuronic acid
glutethimidum glutethimide	3-ethyl-3-phenyl-2,6-dioxo-piperidine
halothanum halothane	2-bromo-2-chloro-1,1,1-trifluoroethane
hexetidinum hexetidine	bis-1,3-(β-ethylhexyl)-5-methyl-5-aminohexahydropyrimidine
hexocyclii methylsulfas hexocyclium methylsulfate	*N*-(β-cyclohexyl-β-hydroxy-β-phenylethyl)-*N'*-dimethylpiperazinium methylsulfate
histapyrrodinum histapyrrodine	*N*-pyrrolidylethyl-*N*-phenylbenzylamine
homarylaminum homarylamine	*N*-methyl-5-aminoethyl-1,2-methylenedioxybenzene
hydrocortamati hydrochloridum hydrocortamate hydrochloride	17-hydroxycorticosterone 21-diethylaminoacetate hydrochloride
hydroxyzinum hydroxyzine	1-(*p*-chlorobenzhydryl)-4-[2-(2-hydroxyethoxy)-ethyl] piperazine
injectio insulini zinci globinati globin zinc insulin injection	a sterile buffered suspension of insulin with zinc chloride and globin
injectio insulini zinci protaminati protamine zinc insulin injection	a sterile buffered suspension of insulin with zinc chloride and protamine
isometheptenum isometheptene	2-methylamino-6-methylhept-5-ene
isothipendylum isothipendyl	10-(2-dimethylamino-2-methylethyl)-1-azaphenothiazine
lauralkonii chloridum lauralkonium chloride	*p*-laurylphenyloxyethyl-benzyl-dimethylammonium chloride
leucovorinum leucovorin	5-formyl-5,6,7,8-tetrahydropteroyl-glutamic acid
levomoramidum levomoramide	*l*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine
liothyroninum liothyronine	*l*-4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenylalanine
magnesii aluminii glycinas magnesium aluminium glycinate	hydroxy aluminium magnesium amino-acetate
mecamylaminum mecamylamine	3-methylamino*iso*camphane
mephenterminum mephentermine	*N*-α-α-trimethyl-β-phenylethylamine

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
meprobamatum meprobamate	2-methyl-2-propyl-propane-1,3-diol dicarbamate
mercaptopurinum mercaptopurine	6-purinethiol
mesuximidum mesuximide	1,3-dimethyl-3-phenyl-2,5-dioxo-pyrrolidine
methallenestrilum methallenestril	3-(6-methoxy-2-naphthyl)-3-ethyl-2,2-dimethylpropionic acid
methituralum methitural	5-methylthioethyl-5-(2-pentyl)-2-thiobarbituric acid
methocidinum methocidin	hydroxymethylgramicidin
methopromazinum methopromazine	2-methoxy-10-(3-dimethylaminopropyl) phenothiazine
methoxyphedrinum methoxyphedrine	1-*p*-methoxyphenyl-1-methylamino-propan-1-one
methylphenidatum methylphenidate	α-phenyl-α-(2-piperidyl)-methyl acetate
methyprylonum methyprylon	3,3-diethyl-5-methylpiperidine-2,4-dione
midamalinum midamaline	*N*-(5-chloro-2-benzimidazolylmethyl)-*N*-phenyl-*N'*,*N'*-dimethyl-ethylene-diamine
monobenzonum monobenzone	monobenzyl ether of hydroquinone
morpheridinum morpheridine	morpholinoethyl*nor*pethidine
natrii calcii edetas sodium calcium edetate	calcium chelate of the disodium salt of ethylenediamino-*N*,*N*,*N'*,*N'*-tetra-acetic acid
natrii dioctylis sulfosuccinas sodium dioctyl sulfosuccinate	di-β-ethylhexyl sodium sulfo-succinate
natrii diprotrizoas sodium diprotrizoate	sodium 3,5-dipropionylamino-2,4,6-triiodobenzoate
natrii radiochromas (^{51}Cr) sodium radiochromate (^{51}Cr)	anionic hexavalent radioactive chromium (^{51}Cr) in the form of sodium chromate
natrii radiophosphas (^{32}P) sodium radiophosphate (^{32}P)	radioactive phosphorus in the form of a mixture of sodium dihydrogen phosphate and disodium hydrogen phosphate
nidroxyzonum nidroxyzone	5-nitro-2-furaldehyde 2-(2-hydroxyethyl) semicarbazone
nitricholinii perchloras nitricholinium perchlorate	2-hydroxyethyltrimethylammonium nitric acid ester perchlorate
norethandrolonum norethandrolone	17-α-ethyl-17-hydroxy-19-*nor*-4-androsten-3-one
norethisteronum norethisterone	17-α-ethinyl-19-*nor*-4-androsten-17-β-ol-3-one
novobiocinum novobiocin	an antibiotic substance obtained from cultures of *Streptomyces spheroides*, or the same substance produced by any other means

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
nystatinum nystatin	an antibiotic substance obtained from cultures of *Streptomyces noursei*, or the same substance produced by any other means
oleandomycinum oleandomycin	an antibiotic substance obtained from cultures of *Streptomyces antibioticus*, or the same substance produced by any other means
ostreogrycinum ostreogrycin	an antibiotic substance obtained from cultures of *Streptomyces ostreogriseus*, or the same substance produced by any other means
oxeladinum oxeladin	diethylaminoethoxyethyl-α,α-diethyl-phenyl acetate
oxycinchophenum oxycinchophen	3-hydroxy-2-phenylquinoline-4-carboxylic acid
pentacynii chloridum pentacynium chloride	*N*-[*N'*-(5-cyano-5,5-diphenylpentyl)-*N'*-dimethylammoniumethyl]-*N*-methylmorpholinium dichloride
pentoxyverinum pentoxyverine	2-(2-diethylaminoethoxy)-ethyl 1-phenyl-*cyclo*pentane-1-carboxylate
petrichloralum petrichloral	pentaerythritol chloral
phenaglycodolum phenaglycodol	2-*p*-chlorophenyl-3-methylbutane-2,3-diol
phenamazolinum phenamazoline	2-anilinomethylimidazoline
phenmetrazinum phenmetrazine	2-phenyl-3-methyl-morpholine
phenobutiodilum phenobutiodil	α-(-2,4,6-triiodophenoxy)-butyric acid
phenoxybenzaminum phenoxybenzamine	*N*-phenoxy*iso*propyl-*N*-benzyl-β-chloroethylamine
phenoxymethylpenicillinum phenoxymethylpenicillin	an antibiotic in which the benzyl group of benzylpenicillin has been replaced by a phenoxymethyl group
phensuximidum phensuximide	1-methyl-3-phenyl-2,5-dioxo-pyrrolidine
phenythilonum phenythilone	2-ethyl-2-phenyl-thiamorpholine-3,5-dione
phenyltoloxaminum phenyltoloxamine	2-(*o*-benzylphenoxy)-ethyldimethylamine
phthalylsulfamethizolum phthalylsulfamethizole	5-phthalylsulfanilamido-2-methyl-1,3,4-thiadiazole
pimetremidum pimetremide	*N*-methyl-*N*-(β-picolyl)-tropamide
pipenzolati bromidum pipenzolate bromide	*N*-methyl-*N*-ethyl-3-piperidinium benzilate bromide
piperazini calcii edetas piperazine calcium edetate	a chelate produced by reacting edetic acid with calcium carbonate and piperazine
piperidolatum piperidolate	*N*-ethylpiperid-3-yl diphenylacetate

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
pipradrolum pipradrol	α,α-diphenyl-α-piperid-2-yl-methanol
polymyxinum B polymyxin B	an antibiotic substance obtained from cultures of *Bacillus polymyxor*, or the same substance produced by any other means
prednisolonum prednisolone	Δ^1-dehydro-hydrocortisone
prednisonum prednisone	Δ^1-dehydrocortisone
probenecidum probenecid	*p*-(di-*n*-propylsulfamoyl) benzoic acid
prochlorperazinum prochlorperazine	1-[3-(2-chloro-10-phenothiazinyl)-propyl]-4-methylpiperazine
prodeconii bromidum prodeconium bromide	*N,N,N′,N′*-tetramethyl-*N*-*N′*-bis-(carbo-propoxymethyl)-2,13-dioxatetradecane-1,14-diammonium dibromide
promazinum promazine	10-(3-dimethylaminopropyl) phenothiazine
promoxolanum promoxolane	2,2-di*iso*propyl-4-hydroxymethyl-1,3-dioxolane
propanocainum propanocaine	3-diethylamino-1-phenylpropyl benzoate
propazolamidum propazolamide	2-propionamido-1,3,4-thiadiazole-5-sulfonamide
propylhexedrinum propylhexedrine	1-*cyclo*hexyl-2-methylaminopropane
prothipendylum prothipendyl	10-(3-dimethylaminopropyl)-1-azaphenothiazine
proxymetacainum proxymetacaine	β-diethylaminoethyl-3-amino-4-propoxy-benzoate
pyridostigminum pyridostigmin	dimethylcarbamic ester of 1-methyl-3-hydroxpyridine
pyrvinii chloridum pyrvinium chloride	6-dimethylamino-2-[2-(2,5-dimethyl-1-phenyl-3-pyrryl)-vinyl]-1-methyl-quinolinium chloride
racemoramidum racemoramide	*d,l*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine
rescinnaminum rescinnamine	3,4,5-trimethoxycinnamic acid ester of methyl reserpate
spiramycinum spiramycin	an antibiotic substance obtained from cultures of *Streptomyces ambofaciens*, or the same substance produced by any other means
streptodornasum streptodornase	enzyme obtained from cultures of various strains of *Streptococcus hemolyticus* and capable of hydrolysing desoxyribonucleoproteins
streptokinasum streptokinase	co-enzyme obtained from cultures of various strains of *Streptococcus hemolyticus* and capable of changing plasminogen into plasmin
streptovarycinum streptovarycin	an antibiotic substance composed of several related components obtained from cultures of *Streptomyces variabilis*
suspensio insulini cum zinco insulin zinc suspension	a sterile buffered mixture of insulin zinc suspension (amorphous) (30 per cent.) and insulin zinc suspension (crystalline) (70 per cent.)

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
tetryzolinum tetryzoline	2-(1,2,3,4-tetrahydronaphth-1-yl)-2-imidazoline
thenalidinum thenalidine	1-methyl-4-[*N*-(2-thenyl)-anilino]-piperidine
thyrotrophinum thyrotrophin	thyrotrophic hormone
tolbutamidum tolbutamide	*N*-p-tolylsulfonyl-*N'*-*n*-butyl-carbamide
tolproninum tolpronine	1-(1,2,3,6-tetrahydropyridino)-3-*o*-tolyloxypropan-2-ol
tridihexethyli iodidum tridihexethyl iodide	3-hydroxy-3-phenyl-3-*cyclo*hexyl-propyltriethylammonium iodide
trimeperidinum trimeperidine	1,2,5-trimethyl-4-phenyl-4-propionoxypiperidine
trimetaphani camphorsulfonas trimetaphan camphorsulfonate	*d*-3,4-(1,3-dibenzyl-2-keto-imidazolidino)-1,2-trimethylene thiophanium *d*-camphorsulfonate
triprolidinum triprolidine	*trans*-1-(pyrid-2-yl)-3-pyrrolidino-1-*p*-tolylprop-1-ene
vancomycinum vancomycin	an antibiotic substance obtained from cultures of *Streptomyces orientalis*, or the same substance produced by any other means
verazidum verazide	1-*iso*nicotinoyl-2-veratrylidene hydrazine
zoxazolaminum zoxazolamine	2-amino-5-chlorobenzoxazole

Annex 1

PROCEDURE FOR THE SELECTION OF RECOMMENDED INTERNATIONAL NON-PROPRIETARY NAMES FOR PHARMACEUTICAL PREPARATIONS *

The following procedure shall be followed by the World Health Organization in the selection of recommended international non-proprietary names for pharmaceutical preparations, in accordance with the World Health Assembly resolution WHA3.11:

1. Proposals for recommended international non-proprietary names shall be submitted to the World Health Organization on the form provided therefor.

2. Such proposals shall be submitted by the Director-General of the World Health Organization to the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated for this purpose, for consideration in accordance with the " General principles for guidance in devising International Non-proprietary Names ", appended to this procedure.[1] The name used by the person discovering or first developing and marketing a pharmaceutical preparation shall be accepted, unless there are compelling reasons to the contrary.

* Text adopted by the Executive Board in resolution EB15.R7 (*Off. Rec. Wld Hlth Org.*, 60, 3)
[1] See Annex 2, page 111.

3. Subsequent to the examination provided for in article 2, the Director-General of the World Health Organization shall give notice that a proposed international non-proprietary name is being considered.

A. Such notice shall be given by publication in the *Chronicle of the World Health Organization* and by letter to Member States and to national pharmacopoeia commissions or other bodies designated by Member States.

(i) Notice may also be sent to specific persons known to be concerned with a name under consideration.

B. Such notice shall:

(i) set forth the name under consideration;

(ii) identify the person who submitted a proposal for naming the substance, if so requested by such person;

(iii) identify the substance for which a name is being considered;

(iv) set forth the time within which comments and objections will be received and the person and place to whom they should be directed;

(v) state the authority under which the World Health Organization is acting and refer to these rules of procedure.

C. In forwarding the notice, the Director-General of the World Health Organization shall request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the proposed name during the period it is under consideration by the World Health Organization.

4. Comments on the proposed name may be forwarded by any person to the World Health Organization within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization.*

5. A formal objection to a proposed name may be filed by any interested person within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization.*

A. Such objection shall:

(i) identify the person objecting;

(ii) state his interest in the name;

(iii) set forth the reasons for his objection to the name proposed.

6. Where there is a formal objection under article 5, the World Health Organization may either reconsider the proposed name or use its good offices to attempt to obtain withdrawal of the objection. Without prejudice to the consideration by the World Health Organization of a substitute name or names, a name shall not be selected by the World Health Organization as a recommended international non-proprietary name while there exists a formal objection thereto filed under article 5 which has not been withdrawn.

7. Where no objection has been filed under article 5, or all objections previously filed have been withdrawn, the Director-General of the World Health Organization shall give notice in accordance with subsection A of article 3 that the name has been selected by the World Health Organization as a recommended international non-proprietary name.

8. In forwarding a recommended international non-proprietary name to Member States under article 7, the Director-General of the World Health Organization shall:

A. request that it be recognized as the non-proprietary name for the substance; and

B. request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the name, including prohibiting registration of the name as a trade-mark or trade-name.

Annex 2

GENERAL PRINCIPLES FOR GUIDANCE IN DEVISING INTERNATIONAL NON-PROPRIETARY NAMES

1. Names should, preferably, be free from any anatomical, physiological, pathological or therapeutic suggestion.

2. An attempt should first be made to form a name by the combination of syllables in such a way as to indicate the significant chemical groupings of the compound and/or its pharmacological classification. Preference should be given to the following syllables:

Latin	English	French	
inum	ine	ine	for alkaloids and organic bases
inum	in	ine	for glycerides and neutral principles
olum	ol	ol	for alcohols and phenols (-OH group)
alum	al	al	for aldehydes
onum	one	one	for ketones and other substances containing the CO group
enum	ene	ène	for unsaturated hydrocarbons
anum	ane	ane	for saturated hydrocarbons
cainum	caine	caïne	for local anaesthetics
mer	mer	mer	for mercurial compounds
sulfonum	sulfone	sulfone	for sulfone derivatives
quinum	quine	quine	for antimalarial substances containing a quinoline group
crinum	crine	crine	for antimalarial substances containing an acridine group
sulfa	sulfa	sulfa	for derivatives of sulfanilamide
dionum	dione	dione	for anti-epileptics derived from oxazolidinedione
toinum	toin	toïne	for anti-epileptics derived from hydantoin
stigminum	stigmine	stigmine	for anticholinesterases

3. Names should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names already in use.

4. The addition of a terminal capital letter or number should be avoided as far as possible.

5. Names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or already officially adopted in any country, or used in the national pharmacopoeias, or in works of reference such as " New and Non-official Remedies ", should receive preferential consideration.

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